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ARCHIVES OF NEUROLOGY AND PSYCHIATRY

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Archives of Neurology and Psychiatry

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INTER-RELATIONS OF THE DOMAIN OF NEUROPSYCHIATRY *

ADOLF MEYER, M.D.

BALTIMORE

The fact that the American Neurological Association entrusted to me the chairmanship of this forty-eighth annual meeting places on me the responsibility of opening the session with some pertinent remarks. I would have these take the form of an attempt to answer a question which I consider of great importance to us, namely: How can we state clearly and simply what constitutes the field of neuropsychiatry?

At this time there is especial need for clearness on this subject. Ours has always been a very responsible field, but today it is all the more responsible since the war has added large numbers of victims of neuropsychiatric disorders. Members of this organization, among them Thomas W. Salmon and our much lamented Pearce Bailey, shaped a definite neuropsychiatric domain. For the first time in the history of the country psychiatrists and neurologists cast their lot together in a remarkable unitary organization. Noteworthy immediate services were rendered at the front and in this country during the war. Now, as lies in the nature of our field, we shall for years to come have to help maintain a worthy follow-up service for the country and for the men and women who rose to meet the great emergency. What can be held out to the public and to the medical profession as the foundation, scope and goal of neuropsychiatry?

THE DOMAIN OF NEUROPSYCHIATRY

The task is not only the care of paralyzed legs and arms and troublesome nerve growths and brain lesions accompanied by impaired speech and other disorders; it is especially the so-called mental aspect, including the understanding of the *person;* of that aspect of the person which is likely to guide *or* misguide public opinion—that which constitutes the moods and morale of the patients, and the willingness and capacity to accept and use assistance, and to develop a real *conscience* about *health.* All this is the domain of neuropsychiatry.

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* President's address read at the Forty-Eighth Annual Meeting of the American Neurological Association, May, 1922, Washington, D. C.

My principal appeal in an effort to formulate a generally intelligible and yet scientifically valid and practically suggestive delineation of the main aspects of our work leads me to the following considerations:

Every domain of medicine has, generally speaking, two problems: the study and management of the special *organ or function* on its own ground, and the study and management of the patient as an *individual personality* and member of a group, as it affects the special organ or function.

Neuropsychiatry is quite specifically responsible in both lines, because the very organ of concern to us is also the principal organ for the integration of the individual as a personality. It is, however, equally essential that we should recognize that some familiarity with the science of man as a personality is as necessary for the gastro-enterologist or surgeon or any physician or student of any problems pertaining to man, as it is for the psychiatrist and neurologist. But it behooves the neuropsychiatrist to know the psychobiologic methods and facts especially well, because he deals with the principal integrating organ. Unfortunately, there are many who want to make a puzzle out of this simple proposition.

My principal claim is that there is no call for the traditional attitude of bewilderment over how to fit the personality-facts into the scheme of objective sciences and practical medical data. The interesting reasons for the difficulty of physicians and laity in the presence of psychiatry, so admirably outlined by Lewellys F. Barker in his Bloomingdale address [1] and what we note from our own experience, resolve themselves into this: There is too much of the bad habit of expecting that the mental problems and mental conditions should be intelligible out of one's understanding of mere words and ponderings, when, as a matter of fact, one should have some first-hand experience with real and tangible human reactions and life factors and the methods of work with them.

THE PATIENT AS A UNIT

It so happens that the leaders of medical organizations largely familiar only with other aspects, such as bacteriology, i. e., facts outside of man, and with physiopathologic part-functions, have treated with undue suspicion the effort of those who see in psychology frankly and directly the study of the patient as a unit or personality, and we find ourselves today confronted with the demands of an intelligent public to furnish trained neuropsychiatrists fit to be social psychiatrists and neuropsychiatrists, with the alternative that the public may have to go elsewhere, outside of medicine, for help.

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1. Barker, L. F.: Psychiatry in General Medicine: A Psychiatric Milestone. Bloomingdale Hospital Centenary. Privately printed by the New York Hospital, 1921, pp. 59-75.

Neglect of the simple common-sense way of recognizing the study of the function of the whole individual or the patient in addition to the function of the parts is largely responsible for much confusion on the part of the medical profession and the public, whereas, as I hope to show, its recognition in terms of plain critical common-sense gives us a sound approach, scientifically and logically, on safe ground and standing the test of direct and simple applicability, objective and constructive.

Unfortunately the public, and even the medical profession, gropes for unsound types of psychology and many a would-be neuropsychiatrist is apt to talk confusingly to the profession and to the public. A frank acceptance of psychology as the study and control of the functions and behavior of the individual organism as a unit or personality gives us a perfectly sound objective basis and sound methods of procedure. The concept of integration and the understanding of the principle of symbolization give us the orderly natural-history view of man which allows us to do justice to the whole personality and the parts, and to the demands of sound medical and hygienic practice.[2]

The principle is not difficult to grasp. We find that the universe of which we are a part presents a vast problem of science, that is, of systematic formulation and experimental and practical control. The all-pervading realm of fact and of method of approach is that of physics and chemistry. But the masses or entities we meet are specifically integrated. From a certain level of complexity, they show more or less individuation and constitute finally what we call biologic units and groups of units. The special types of this whole large group can be presented in terms of a fraction, the denominator being the formulation of the facts of life in general—metabolism, growth and organization and reproduction. The numerator is one or another type or degree of development of the general biologic type: the purely vegetative type with only limited and incidental motion; then the branch of life characterized by motion and all that which goes with the animal type of life forming the numerator of our fraction. Within this we have first the forms with a type of behavior possible without a nervous system, and other forms in which the numerator crystallizes a definite nervous system with a literal *organization* of *reflex* process. It is within this that another specialization occurs, namely, that of symbol activity and what in ourselves we know and describe as integration in more or less of consciousness. The swinging in of a nervous system brings us an organ working essentially as an integrator, with no special meaning and value as such, remarkably economizing, little energy-consuming and

2. Contributions of Psychiatry to the Understanding of Life Problems, in A Psychiatric Milestone, pp. 21-54.

with little fatigability, unable to live and work by itself but serving the task of unification in the form of reflexes and their combinations. On this ground, among the many exigencies of life there expands a special type of *organization not only of structure but specifically of function,* an organization in what we know as more or less "conscious" *activity.* This organization takes place through that tremendous development which has as its essence the *use of symbols,* or symbolization, in the form of sensation standing for certain facts, perception and images, memories, picture-formation, and language, all unified in subject-organization and psychobiologic integration. Thus human behavior becomes the behavior of an integrated individual brought into psychobiologic organization with the help of all that which makes up man's specifically "mental" equipment and symbolizing or representative reactions hanging together in more or less consciousness. This realm of function is justly combined into a special topic of psychology or psychobiology, in contrast to or in addition to the science of *reflexes* which do not involve symbolization, and do not depend on integration with the help of signs. But in distinction from tradition we do not treat the "mental" or "conscious" data as a detached and special purely subjective realm of facts; we study them as a special incident of the objectively observable behavior.

As soon as sensations and perceptions, memories, images and ideas, fancy and reasoning, forecasting and deliberation, are involved in reaction and actions, we find a type of function or behavior which constitutes itself as "function or behavior of the *individual,*" in what I call *subject-organization,* not merely as an abstract mind, as tradition has it, but as a specifically integrated type of activity of the cerebrally integrated *organism;* not as a part of a detached world but as the natural form of a psychobiologically integrated life and behavior—physics and chemistry, if you please, but biologically, vegetatively, reflexly and psychobiologically integrated physics and chemistry, not only dealing with new words but with specific functions and coordinations and discriminations of behavior of definite kinds of organisms. Psychobiologically integrated activity, or behavior with the help of *mentation,* or we might say in an even more telling manner, "behavior with the help of *imagination,*" implies naturally and inevitably this new development: the inclusion or insertion in the *reflex-type* of function, of *symbolizing functions* of the highest possible saving in energy consumption; it *implies* the *"mental" activity,* which, however, is definitely recognized as cerebrally integrated activity of the organism, but making possible a *new "state of function,"* the organization as an "individual in action as an agent or subject," as the "he" or "she," the "you" or "I" we know as a biologic individual and social entity. Just as *metabolism*

constitutes the special feature of the domain of physics and chemistry that makes up biology, so *symbolization*, the development of sign-function, establishes the psychobiologically integrated types of organism and function. Instead of acting as an ordinary mechanistic reflex-machine, the organism constitutes itself as a *subject*, with all the mind and soul that our anthropomorphic parlance chooses to emphasize, attained through the incorporation of symbolization among the other biologic or life-dependent functions and activities.

SYMBOLIZATION

The concept of symbolization, that is, treating the mentally integrated states and activities as brought about with the help of sign activity and its organization, is not difficult to grasp. It shows in the production of sign reactions from simple sensations up, that is, activity not necessarily of any special potency of effectiveness by itself through the actual physical energy-display it contains or implies, but *getting its meaning and potency through its service in an associative system*, a system which constitutes itself concretely as the variously adapted *subject or personality*. It shows in part individually and in part socially, as in the form of gesture, emotional display and language and their silent forms, built up out of perceptive-cognitive-discriminative and affective and conative assets of response and construction. It brings about something that activity *not* integrated with this help could not produce with such a degree of differential adaptation. Just as logarithms and algebraic notations bring in simplifications and new possibilities of operation, so the introduction of the sensory-cognitive and conative and affective assets in overt form or overt behavior, or in their economizing so-called "mental" type experienced as mental activity or mentation, gives us means of psychobiologic integration, so remarkably organized as *using on the same level reality and fancy, past, present and future, one's own ideas and those of others, in overt effective and expressive action* or in the specifically economizing form of implicit symbolization.

Jelliffe and White in their "Textbook of Neurology and Psychiatry" recognize this formulation and give us the data of neuropsychiatry in three long chapters on the physico-chemical systems with the *vegetative* nervous system, the *sensorimotor* systems, and the psychic or *symbolic* systems. They give us a very concise and essentially American conception in a pithy paragraph (p. 21): "The *hormone* is the type of tool at the physico-chemical level, the *reflex* at the 'sensori-motor' level, and finally the *symbol* at the psychic level." My own conceptions are very similar, only I prefer to speak outright of the vegetative, the reflex and the psychobiologic types of function or levels, and I prefer to claim

as frankly unnecessary the confusing contrast of physical and psychic, as indicated in various older discussions of mine.[3]

We have, then, a formulation of the facts we deal with that keeps us on the ground of *objective data,* with our eyes clearly open to the specific precautions needed in this field of relativities, with methods correspondingly adapted and safeguarded and without any call for mystical notions on the one hand or neurologizing psychophobia so confusing to common sense on the other hand.

With such a philosophical and practical conception, one learns to subordinate the exaggerated contrast of mind and body, and to speak of reactions of the internal or visceral organs, the nervous segmental and suprasegmental organs and functions as such, or as parts of the reactions of the cerebrally integrated *person.* The nightmare of neuropsychiatric dilemma has no place. What the patient does, feels and thinks ceases to be made a puzzle; one either finds objective facts calling for one's attention or one does not.

How do these general conceptions present themselves concretely? Our objective psychobiology expresses itself concretely and simply in certain definite aims in our medical curriculum. It is my ambition to organize the essentials as a scheme of neuropsychiatric work that will give us a right to insist on a comprehensive picture of the entire domain and on absolute clearness of the essential *lines* so that they may become usable in *all* medical practice. All our medical schools of today train the student to include a minimal number of neurologic routine tests in any medical examination. But how many medical teachers of today and how many neurologists make it an acknowledged practice to include planfully the minimal number of questions and tests that will draw out the reactions disclosing at least the most tangible psychobiologic problems? There is no difficulty in this. One simply has to be at least as familiar with *some ordinary human problems and standards of adaptation* as one is with the facts of reflexes, ataxia, tremor and palsies, anesthesias and decerebrate rigidity and fits. After testing the principal reflexes, one should ascertain how the patient reacts and responds to a minimal number of simple questions: What difficulties do you want help for? What is your work and how does it agree with you? Have you had any special experiences, or moods or fancies, fears or worries, or imaginations which you could not throw off? Does fate and everybody treat you all right? How does your memory serve you?

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3. Especially in the review of Moebius: The Hopelessness of All Psychology, Psychol. Bull. **4:** No. 6 (June 15) 1907; an article in J. Insanity **65:** pp. 39-52; and in a later article that may have sounded strange with its provocative title: "Objective Psychology or Psychobiology with Subordination of the Medically Useless Contrast of Mental and Physical," J. A. M. A. **65:**860 (Sept. 4) 1915.

Wherever evidence calls for it, a small number of performance tests give us the memory data.

We add today to a reasoned scheme of working in anatomic and clinical neurology a gradual working out of a general and special psychobiology and psychopathology for the student, beginning with the technic and practice of the simple life-study of an average person and average problems of psychobiology, and extending it to the work with the fundamental reaction-types and problems of psychopathology and psychiatry.

Instead of considering psychiatry a field of asylum diseases, let us see what we find wrong in behavior and mentation, without damning it at the outset by a terminology derived from merely possible terminal developments. The personality-reactions present themselves to us concretely in terms of reaction-groups: mood disorders, fears, obsessions, states of panic, seclusiveness, fancy states, simple or disorganizing, and memory, retention, judgment and behavior disorders—plain facts which do not necessitate any very learned or bewildering vocabulary. We look for concrete mismanagement of home situations, for discrepancies of ambition and performance, existing difficulties and failures, problems of adaptation and problems of desensitization; and doing so, we shall be helpful to our patient instead of sacrificing him at the altar of vocabularies dealing with terminal states and with fixed fatalistic "constitutions" and too dogmatically fixed "disease entities."

THE SCOPE OF THE EXAMINATION

We must get away from the idea that one examines only for some all-inclusive asylum diseases like dementia praecox and manic-depressive insanity and paresis. One examines primarily for the range of personal capacity to help in an examination and to cooperate in any plan for treatment, that is, assets as shown in plain life problems and successes and failures. If there *are* any failures, one determines whether there are any toxic or infectious intruders, any disorders of the internal organs and their functions, any neurologic disorders (including the suprasegmental as well as the segmental symptoms); and finally any disorders of behavior or of mental reactions, not in the abstract but in terms of what the patient does with the jobs, with the family, with other people, and with his own worries, and feelings, and notions and moods, the thoughts he cannot throw off, the memory and judgment, and the speech and writing, and the management of his eliminative functions and sleep and appetite. One does not fish merely for a few so-called "frontal lobe symptoms."

I am more concerned with having the best possible understanding of the condition and needs of the patient at the *time*, than with the customary relatively uncertain guesses as to the ultimate fate. I want

to make sure that my attention is focused on all the points which might make a difference in the immediate treatment and guidance of the patient, *without* therefore losing sight of the long-term problems, the future and the ultimate fate. In some conditions, such as delirium, agitation, depression, or states of panic, the immediate problems are as clear and urgent as in any acute disease of general medicine; in other cases the broad long-term problems must lead us rather than the immediate appearance, as in the temporary spurts or temporary improvements of paresis or of paranoic or deterioration or psychoneurotic states. In all cases we need a sane elastic balancing of the facts, and I feel that we can show that this is possible with a theoretically and practically sound scheme, without leading the student first through a stage of dogmatic cocksureness of ultimately unattainable nosology and general pathologic assumptions.

I am told that when I outlined a similar point of view at the Bloomingdale centenary, one of our colleagues turned to his neighbor with the remark: "How is this to help us in a case of brain tumor?" It is true I did not then discuss brain tumors specifically, but the "Contributions of Psychiatry to the understanding of Life Problems." But does not the plan of attack bring a certain clearness into the study of any patient? Assume that even the brain tumor patient, like E. W. Taylor's case, is one who has for years been troubled by obsessions; or that the condition is one of a korsakow-like collosal syndrome. In the former case we must know that the mental disorder is *not*, and in the latter that the mental disorder *is*, naturally accounted for by a focal disorder. In either case an examination and study of the facts as we find them in mental or psychobiologic terms are necessary before we dismember the data.

It is clearly important that we should guide the public to recognize quite frankly a call for an obligatory practical pluralism in the use of the facts and methods required in the understanding and treatment of our patients. The layman understands at once what we mean by a study of the special organs and the study of general conduct and behavior and mentally organized functions. We study not an abstract "mind" but the functions and *activities* which constitute the facts of mind—just as we might study water and not "wetness," and living *things* and not life as a detached problem. To be sure, the public with its ideas of a detached mind is today as much as ever under the influence of one-sided fads, all kinds of one-sided faith-healing, and all kinds of temporarily successful cults; even physicians send patients deliberately and without further guidance to the healing cults and to consultants and healers inadequately trained—apparently without knowledge of or trust in the conscientious efforts of physicians with all-round training. As a compensatory reaction still others refer the public to a one-sided

infection theory, or to a one-sided endocrinology, or the patient takes refuge with the osteopath or other types of chiropractor's work because of their grossly tangible display of curative efforts—their doing something with their hands, that which gives the surgeon his name. Our responsibility is great. As neurologists let us profess frankly that we are *really neuropsychiatrists,* that is, physicians with a comprehensive scope of interests and methods; and let us also see to it that the spreading of frank and intelligible views of the nature of the life problems and the psychobiologic symbolizing level becomes a necessary and obligatory concern of the rank and file of physicians, appreciated in its right importance by both physician and patient.

A NEUROPSYCHIATRIC ASSOCIATION

Whether, in view of the practical exigencies, and for the sake of greater clearness in the mind of the public, our Association should, on the occasion of its fiftieth meeting, call itself the American Neuropsychiatric Association, in keeping with the composition of its programs, and in memory of Pearce Bailey and those who did and do the war work, is a question worth raising. This would not mean any submerging of either neurology or psychopathology. There will but rarely be physicians who can cover the whole field, and each investigator will have his own choice of problems. But one thing is certain: We do demand of every one a reasonable training in the *entire domain,* including the functions of the organism constituting the personality. We want neuropsychiatrists—not merely neurologists and not merely psychologists, but primarily physicians able to study the entire organism and its functions and behavior and more especially the share of the nervous system and of the general problems of adaptation.

As we deal with the policy of the care of the war veterans, let us not enhance the inevitable traditional and personal difficulties and confusion among physicians and patients by overemphasizing a split between the neuroses, psychoneuroses and psychoses, and the like. Let us remember that many psychoneuroses as problems of general adaptation are infinitely more problematic and difficult to treat than the frank psychoses. The maintenance of the necessary self-discipline and the practical use of judgment is often much more difficult to obtain in the so-called psychoneuroses. The actual work of study and readjustment requires a high degree of cooperation on the part of the patient. Let us do our best not to give cause for outcries of indifference on the part of the physician through disregard of the personality facts, and for the patient's untimely and arbitrary withdrawal from experienced guidance. Let us see that the policies can be shaped by those who are able to study and master the facts about the parts as well as the personality, by those who know *best* and work *most,* rather than by the sensational magazine

literature and the exploiters of dissension in the neuropsychiatric camps. To attain this we have to be creative and constructive and in the front line, and we cannot trust the old policy of mere following and drifting when we come to the psychobiologic problems. We must travel under one flag and with a clear aim.

There may be a few among us who feel that neurology should maintain its exclusive and dominant attitude by pointing to psychiatry as an extraneous and practically negligible asylum and sanatorium field, and that what can be handled at large should be handled under a vernacular of general medical and neurologic camouflage sparing the public's feelings about the mind. Neither the conscience of the profession nor the state of public opinion can drift profitably in this manner. The most practical step toward the solution of our problem is the rounding off of our training among ourselves and in our general medical curriculums by giving the student and worker good foundations for the simple and every-day tasks of psychobiology and understanding of ordinary personalities and their problems and needs. Let us realize among ourselves that neuropsychiatry stands for making organized and critical medicine a field of work with personalities as well as with the part-organs and functions, and that while there *must* be special workers devoted to special research in the special fields, no physician and no intelligent lay person can afford to disregard the gains by the modern readjustment: the recognition of life problems on the psychobiologic level of integration, the promotion of a training in medicine dealing with the defective and unusual child, the growth of interest in the minor difficulties of human behavior and mentation, and the humanizing of the work with all states and conditions of disease and maladaptation.

You may think me visionary for expecting very much from a broadcast recommendation of apparently a kindergarten measure, yet my long experience convinces me that even simple and practical working habits mean more than long reasoning. In every ordinary medical examination today we require a summary examination of reflexes and fundamental sensorimotor functions, and we now add to this, as equally obligatory, an inquiry into the patient's feeling of content or discontent, mood or spirits, special preoccupations and strains, the sex-adaptations and the essential points of life-problems calling for proper hygienic regulation. We recognize in these inquiries into the assets and tendencies and problems of the personality the basic and necessary rounding off of the study of any patient.

In the patients in whom psychobiologic problems *predominate,* we study the reactions and resources of the person as simply and as fully as we study the reflexes, accepting the data frankly as psychobiologically integrated facts or data of behavior of the individual as a person.

We work with a reasonably limited number of reaction sets, that is, groups of facts that have a specific meaning to us. These may be of

the nature of part-disorders—the irritable weakness type, the anxiety-reactions, the hypochondriacal, the dysmnesic-hysterical, the obsessive-ruminative and the simple defect type of facts; or we consider the more sweeping reaction sets, the thymergastic or affective, the parergastic or twist, the dysergastic or toxic, and the anergastic or organic defect complexes, always remembering that any *one* patient can present *more* than one of these sets of facts. We study the factors entering into the disorders, the poisons and infections (exogenic), the metabolic (organogenic) components, and then the constitutional and the more definitely modifiable and adjustable psychogenic experience-determined factors and special function-tendencies.

The fundamental inter-relations of neurology as the study of the part-functions of the nervous system, and of psychobiology as the study of the total reactions of the individual integrated by the cerebrum, are only one example of the general call for study of the functions of the parts and the functions of the whole.

Since the nervous system forms the essential basis of neurology and psychobiology or personality-function, neuropsychiatry furnishes the general science of man and medicine with the simple as well as the detailed methods needed for the study of structures and parts and the study of the patient as an individual.

In all this we are turning into a planful technic and philosophy that which physicians and patients have always *needed* and physicians have sometimes *practiced*. Neuropsychiatry must work out general methods and principles to be of service in the practice of medicine as a whole; and with growing simplicity and clearness neuropsychiatry may furnish the veteran and the rank and file of humanity a safe and sane conception of human life and its health, and of the range of medical helpfulness.

It is easy to put it quite simply:

We consider it obligatory in the study of the reactions of man not only to test the pupil and patellar reflex, but also a few essential reactions to life problems and the essential ways of using and adapting one's self. Let us trust that such a conception of neuropsychiatry may become a general one in practice and in teaching.

The public will then learn how to use the neuropsychiatrist, and especially how to cooperate and what to expect. That the medical profession appreciates the change is, I believe, adequately shown by the frequency with which not only long mismanaged cases but acute cases are given the benefit of timely neuropsychiatric discussion and study among the junior members of our medical staffs. Let us show the world that even we of the older generation have some of the plasticity and vigor of ever-growing youth.

SUBACUTE EPIDEMIC (LETHARGIC) ENCEPHALITIS*

JOSEPH H. GLOBUS, M.D., AND ISRAEL STRAUSS, M.D.
NEW YORK

In acute epidemic encephalitis the characteristic anatomic changes are perivascular infiltrations, a moderate amount of neuronophagia, a mild degree of glia proliferation and occasionally hemorrhagic foci. These changes are most commonly found in the region of the midbrain and basal ganglions; more rarely other parts of the central nervous system are involved.

But these changes do not exhaust the histopathology of acute epidemic encephalitis. The material studied by the earlier workers was limited to that form of the disease often fatal in its early stage; as material becomes available from cases that have run a more or less protracted course, new findings may be expected.

Economo [1] has reported a case which he called "chronic intermittently progressive lethargic encephalitis." His patient, 45 years of age, insidiously developed atypical lethargic encephalitis, characterized by alternate episodes of delirium and lethargy, dysarthria and the Babinski reflex with no ocular or other palsies or other neurologic signs. For two months the condition remained unchanged, and was then followed by partial improvement. The delirium and lethargy disappeared; the Babinski phenomenon could not be obtained; but dysphagia, paresis of the tongue and choreiform contractions of the extremities appeared. The later course was characterized by alternate improvement and decline in the condition of the patient, death occurring about a year and a half after the onset of the disease.

The histologic changes in the brain stem led Economo to conclude that he was dealing with a chronic epidemic encephalitis, with the addition of an acute process in the terminal stage. The anatomic changes which he considered as incurred during the early, acute period of the disease, were: (*a*) areas of softening with or without accumulation of granular cells; (*b*) bands of dense glia fibers; (*c*) small collections of glia cells, which apparently were at one time concerned with the process of neuronophagia; (*d*) mild degenerative changes in the axis cylinders of long projection tracts. He described recent perivascular hemorrhages, degenerative changes in ganglion cells and perivascular infiltrations, and considered them as evidence of acute recrudescence of the

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1. Economo, C. von: Ein Fall von chronischer schubweise verlaufender Encephalitis Lethargica, München. med. Wchnschr. **46**: (Nov. 14) 1919.

disease. He suggested that this recrudescence was probably due to incomplete elimination of the virus during the early period of the disease, and that a highly suggestive analogy was thus established between chronic progressive muscular atrophy in its relation to acute anterior poliomyelitis, and this chronic form of lethargic encephalitis in its relation to acute epidemic encephalitis. It would appear from the clinical history of Economo's case that an attempt toward healing must have occurred in the course of the disease, but his histologic descriptions fail to show any reparative change in the brain, the lesions described, such as softening, accumulation of granular cells and extravasations, pointing mainly to a lesion of destructive character.

Watson [2] has reported the case of a young woman who suffered for several weeks with insomnia, became extremely anxious about her condition, and fearing that she was going insane, attempted suicide. She was sent to the hospital, where on admission she presented a picture of agitated "melancholia" with suicidal tendencies. For four months her condition remained unchanged. Within the next two months there was improvement in her mental condition, but toward the end of this period she began to complain of pain in the back and left thigh, and was confined to bed. This condition persisted for two months, with progressive development of symptoms, such as inability to speak and paralysis of the right half of the tongue. She fell into a lethargic state, out of which she could easily be aroused to answer questions. A right hemiplegia with anesthesia and analgesia developed eleven days after the onset of paralysis. The deep reflexes were exaggerated and the abdominal reflexes were absent on the paralyzed side. Optic neuritis of moderate intensity developed. She died a week later. The temperature throughout the illness was subnormal; the blood count showed definite leukocytosis.

Necropsy revealed a large area of recent softening with pia adherent in the left cerebral hemisphere. The involved area showed no gross hemorrhages. Microscopically this area showed enormous increase in the vessels, with marked cellular infiltration. The brain stem showed: smaller areas of softening, irregularly distributed throughout the brain substance; marked changes in blood vessels, consisting of infiltration of adventitia with small round cells, polyblasts, epithelioid cells, plasma cells, pseudoplasma cells, thickening of adventitia through proliferation of polyblasts and adventitial cells, swelling and proliferation of intimal endothelium, perivascular hemorrhages, thrombosis of smaller blood vessels, sievelike areas of rarefication about the blood vessels, mild gliosis, but no monster cells. Watson concludes that the changes were more hyperplastic than hemorrhagic in character.

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2. Watson, G. A.: A Case of Encephalitis Lethargica Involving Chiefly the Cerebral Cortex, J. Neurol. & Psychopath. **1**:34 (May) 1920.

Watson demonstrated an important departure from the observations of Economo. We record changes in the central nervous system that indicate a well-defined tendency toward repair, similar in some respects to the changes described by Watson.

Our cases may be grouped clinically with the mild protracted forms and may be termed subacute epidemic encephalitis. Early in the course of the illness the patients showed a well-defined tendency toward recovery, but they eventually passed into an acute and rapidly fatal stage. It was our belief before anatomic studies were made that on the subacute, mild, self-limiting form of the disease, an acute, possibly hemorrhagic, attack was superimposed, causing a fatal issue.

REPORT OF CASES

CASE 1.—*History.*—I. G., a man 53 years of age, a tailor, was admitted to the Mount Sinai Hospital, complaining of double vision, weakness of the left upper and both lower extremities, which had caused several falls, headache and vertigo. His family and personal histories were negative, with the exception of an attack of grip four years previously, when he suddenly developed retention of urine for thirty-six hours. He made an apparently uneventful recovery.

The present illness dated back about six months, when he began to complain of occasional headache and vertigo, not associated with any mental or organic neurologic disturbance. There was no apparent change in personality. The attacks of vertigo were never associated with convulsions. Ten days before admission he complained for the first time of double vision, and a week later, while his eyes were being examined, his knees suddenly gave way, and he would have fallen, but for support. The following day his left hand became weak; he was unable to hold light objects; a day later this weakness became more pronounced, and he could not flex the middle finger of the left hand. The weakness of the lower extremities grew rapidly and progressively worse so that on the two days directly preceding his admission he became extremely unsteady. He fell frequently and had to be assisted to rise.

Physical Examination.—The patient was well developed and well nourished. There was paresis of the lower extremities. He had difficulty in gaining and maintaining the sitting posture. Mentally he appeared alert, showed no impairment of judgment or intelligence, and was normal in his reactions to his surroundings, displaying no unusual irritability or depression. Aside from the neurologic findings he showed no signs pointing to a disturbance of the cardiovascular, respiratory, alimentary or genito-urinary system.

Neurological Findings.—The pupils were normal in outline and in reaction to light and in accommodation. In the left eye there was complete paralysis of the external and internal recti and incomplete paralysis of the superior and inferior recti and superior oblique. In the right eye there was incomplete paralysis of the internal rectus. The fundi were normal. There was weakness of the left orbicularis palpebrarum. Motor power was markedly diminished in all extremities, but more on the left; there was no atrophy or fibrillary twitchings; repeated rapid movements of an extremity caused fatigue without direct recovery of strength on resting. There were myasthenic electric reactions. All deep reflexes were equally increased; the abdominal reflexes were diminished, but equal; there was no clonus; there was a tendency toward

a Babinski sign on the right. Coordination tests could not be carried out because of extreme weakness of the extremities. The spinal fluid was under increased pressure, it contained no cells, a faint trace of globulin, a trace of albumin, and the Wassermann test was negative. The blood Wassermann test was negative. The urine contained no albumin or casts. The temperature remained normal except during the terminal stage, when it reached 100.2 F. The blood pressure was: systolic, 120, diastolic, 75.

Course of Illness.—Soon after admission there was slight improvement. There was some increase in the motor power and the excursions of the left eye increased in range. These findings and the general cheerful attitude of the patient made the outlook appear promising. After five weeks in the hospital, a sudden decline in his condition was shown by increased ptosis, further limitation of eye movements, motor weakness, nasal speech, dysphagia with slight regurgitation and by accumulation of mucus in the nose and throat. During the next and last eight days of the patient's life, the symptoms rapidly became worse. We noted complete bilateral external ophthalmoplegia, extreme paresis of all extremities and paresis of the muscles of mastication. To this were added masklike facial expression, nearly complete dysarthria, inability to swallow, denoting a rapidly advancing bulbar paralysis, culminating in death.

CASE 2.—*History.*—B. B., a girl 18 years of age, a stenographer, was admitted to the hospital on March 9, 1921. The family history had no bearing on the case. The patient gave a history of measles, diphtheria and scarlet fever in childhood. Four weeks before admission she complained of dimness of vision, diplopia associated with slight vertigo and gradually increasing weakness of all the extremities. There were no convulsions or twitchings; sleep was not disturbed, neither was there somnolence. The weakness of the extremities gradually increased so that the patient became fatigued on the slightest exercise. A week before admission she began to have difficulty in swallowing and mastication. There were no cardiac or respiratory complaints.

Physical Examination.—The patient was fairly well developed and not acutely ill. She was confined to bed because of general weakness. Both eyelids drooped, the left slightly more. The right pupil was a trifle larger; both reacted to light and in accommodation. The fundi were normal. There was slight weakness of the external rectus, weakness of both orbiculares palpebrarum, and flattening of both nasolabial folds. The tongue protruded centrally and showed neither tremor nor atrophy. There was an irregularly intermittent tic-like movement of both eyelids. The soft palate did not move in phonation, but palate reflexes were active. Sensation of the face and of the cornea was normal. Muscles of mastication were normal. The patient raised the arms to a right angle with difficulty and could not maintain this position more than a few seconds. The weakness was greatest at the shoulders and the posterior portion of the deltoids was atrophic. The left side seemed to be more severely affected and the deep reflexes at the wrist and elbow were increased on the left. No tremor or ataxia was noted. The muscles of the neck and of the trunk were weak. The lower extremities presented no atrophy or disturbance of tone, but were paretic. The electric muscle reactions were normal. Knee and ankle reflexes were exaggerated, the left slightly more so. There was no clonus and no definite Babinski sign. The abdominal reflexes were normal. The spinal fluid was clear, under normal pressure, and contained no cells; the Wassermann test was negative.

Course of Illness.—The patient's condition remained almost stationary for some time. There were occasional periods of more difficulty in deglutition and phonation, choreiform movements in the arms, and nystagmoid movements. However, at the end of her stay in the hospital she began to show signs of improvement, as she was able to walk about. She was discharged April 23, 1921, as improved, with the neurologic findings but slightly changed. There was no rise of temperature during this period. She remained at home, her condition unchanged until ten days before her second admission, Oct. 9, 1921,

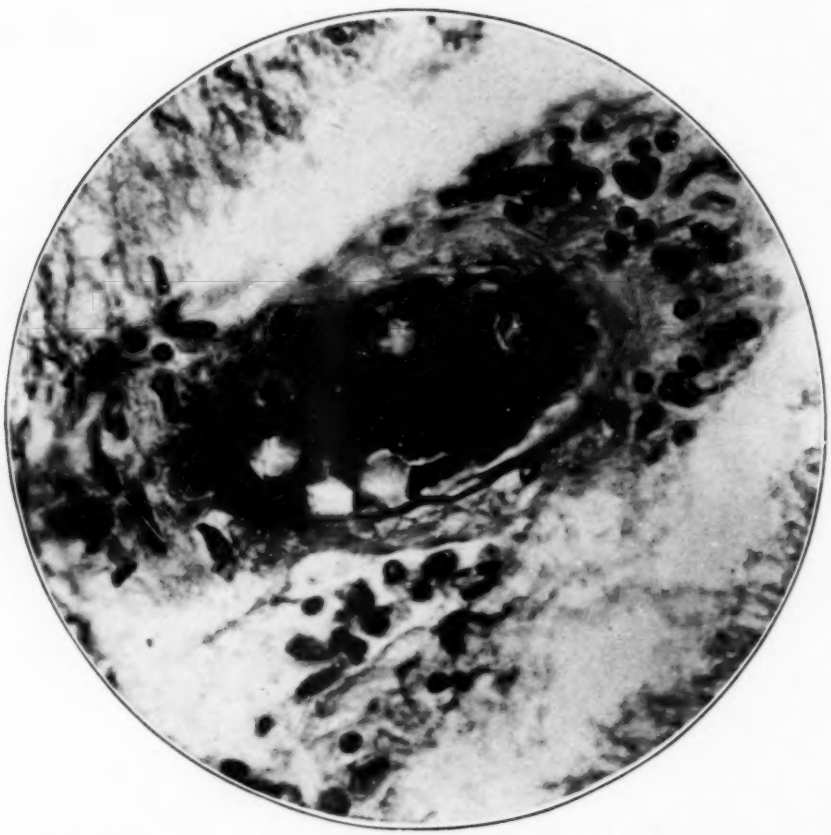

Fig. 1.—Section of the optic thalamus (midbrain). Medium sized vessel showing typical adventitial infiltration.

when she began to complain of headache; pain in the right side of the chest increased on inspiration and cough. She had increasing difficulty in bringing up mucus which accumulated in the throat and tended to choke her. Six days later she became unable to swallow food and had great difficulty in talking. Respiration became labored and difficult. There were no chills, fever or vomiting.

On readmission, the patient appeared acutely ill, breathing with difficulty, with the accessory muscles brought into play. Double ptosis was noted, also clonic-like elevations of the eyebrows. The pupils were widely dilated and fixed, the fundi normal; there was no paralysis of the extrinsic ocular muscles

or nystagmus. There was no sensory disturbance. The deep flexes were normal. The abdominal reflexes could not be elicited. There was a masklike expression of the face. The patient could not protrude her tongue, nor move it from side to side; it was atrophied. She could not swallow; fluids were regurgitated. The palatal reflexes were lost. There was marked dysarthria which gradually led to complete loss of speech. The temperature remained normal. Her condition declined rapidly, and after two days in the hospital she died from respiratory paralysis.

Fig. 2.—Gray substance, lateral to the aqueduct of Sylvius; medium sized vessel, showing early adventitial changes, such as formations of fibroblasts. Various elements of perivascular infiltration are still in evidence. Small lymphocytes, glial cells, granular cells and fibroblasts are among them.

Case 3.—*History.*—M. P., a woman 22, married, developed pain in the lower part of the abdomen and slight vaginal bleeding five months previous to admission. Ectopic gestation was suspected and a laparotomy performed. A bicornate uterus and evidence of early pregnancy in one horn were disclosed. Abortion followed. After discharge from the hospital, the patient's condition remained below par. She complained of frequent headaches and blurred vision for four months preceding the onset of acute symptoms. Two weeks before

admission she suffered from coryza and cough but remained up and about for a few days, when she had a slight chill, followed by a rise of temperature. She was put to bed, and soon showed improvement; two days later she developed high temperature, cough, severe headache, and signs of pneumonia in the left lung. Attacks of vomiting followed, accompanied by delirium and retention of urine. She became somnolent the day before admission.

Physical Examination.—The patient when admitted was comatose and restless. There were no ocular palsies; the pupils were dilated, the left more than

Fig. 3.—Vessel showing the marked increase in adventitia, giving rise to a fibrous scar.

the right; neither reacted to light. The eyes rolled from side to side. There was no asymmetry of the face or rigidity of the neck. The heart was normal; the lungs showed pneumonic signs in both lower lobes. The abdomen was normal. The extremities showed no paralysis and no Kernig or Brudzinski sign, but a slight exhaustible ankle clonus, and a bilateral Babinski sign. The blood picture was negative. The urine was normal, except for a faint trace of albumin. The temperature, from the day of admission to the day of death, rose gradually from 99 to 104.6 F. The spinal fluid was clear, under normal pressure, with 80 lymphocytes per cubic millimeter.

Course of Illness.—On the day after admission the patient remained comatose; there was no definite ocular palsy but a limitation of eye movements to the extreme right and left. The left pupil was larger than the right, and did not respond to light; the right responded only slightly. The fundi were normal. Ptosis was noted, also slight flattening of the lower part of the left side of the face, but no paralysis of the tongue or palate and no rigidity of the neck. The knee and Achilles jerks were not very active. A bilateral Kernig sign and occasional myoclonic movement were noted. On the following day the coma persisted, Cheyne-Stokes respiration developed and death occurred from respiratory paralysis.

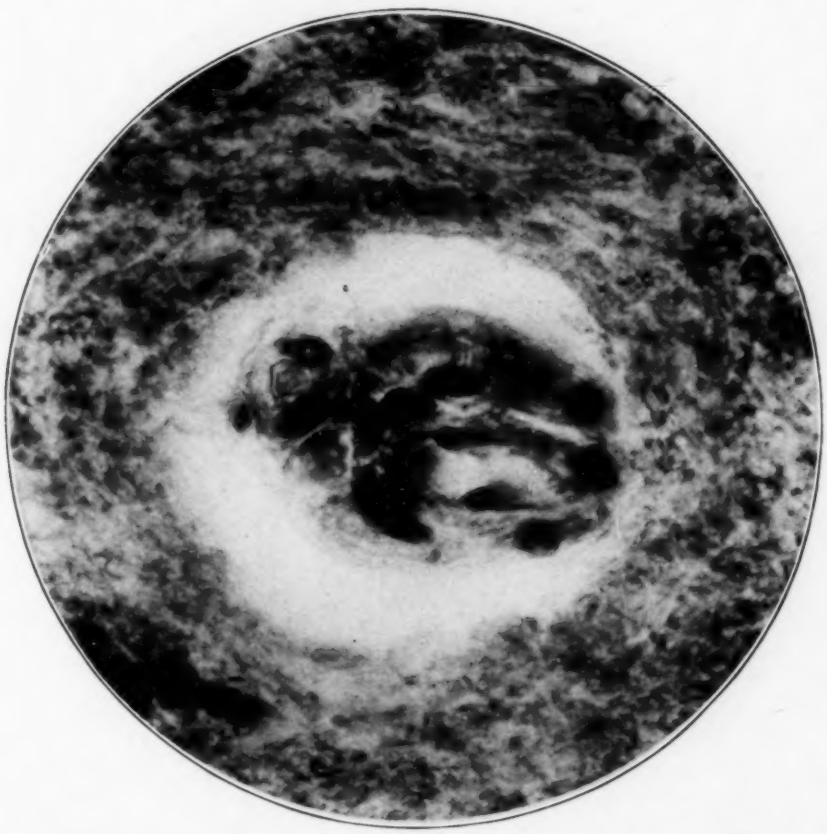

Fig. 4.—Small capillaries; type of vessel found most frequently but not exclusively in the midbrain. About a definitely thickened capillary there is a group of apparently newly formed, patent blood vessels.

Case 4.—*History.*—S. B., a woman 33 years of age, married, was admitted to the hospital on Sept. 10, 1921, complaining of frequent vomiting for over six weeks and cough of one week's duration. The family and previous medical histories were unimportant. Four years before she had been treated for three weeks at the Manhattan State Hospital for neurosis, and a year before had had pneumonia with uneventful recovery.

The repeated vomiting made her think that she was pregnant. The vomitus was occasionally greenish, but never bloody. After two weeks a curettage was performed with no relief. She was able to retain only small amounts of food. There was neither jaundice nor heartburn. A week before admission a persistent cough began with neither hemoptysis nor night sweats. She began to have occasional frontal headaches. It made her dizzy to rise.

Physical Examination.—She was well developed, well nourished and apparently not acutely ill. The chest and cardiovascular system were normal.

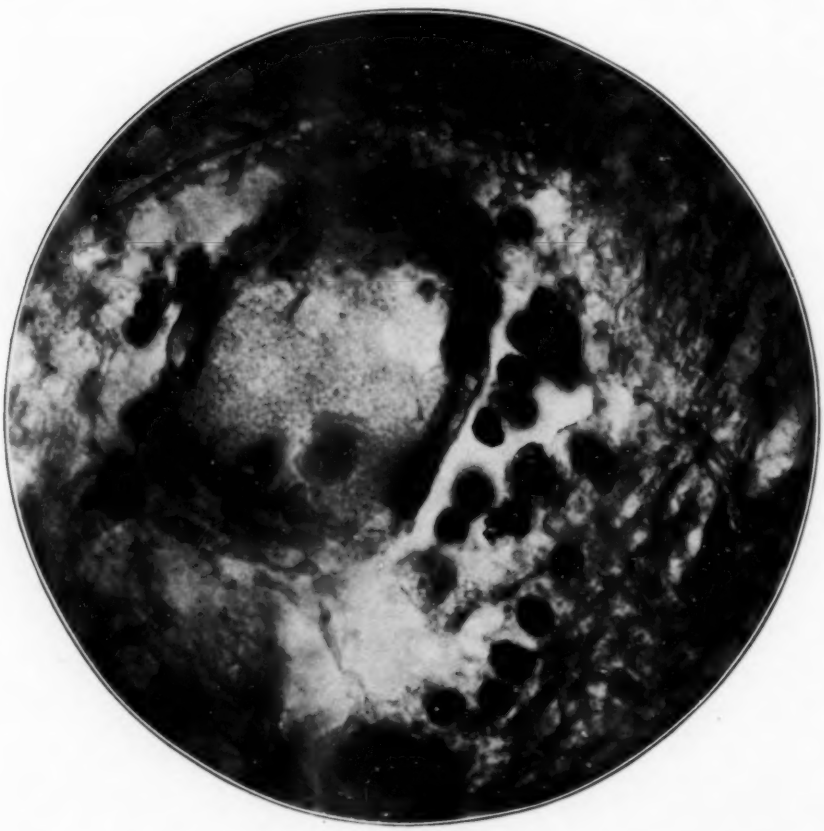

Fig. 5.—Vessel showing reduplication of the endothelial lining. Very close to the vessel there is a collection of glial elements and a few gitter cells.

The abdomen showed practically no abnormal findings. The extremities were normal. The abdominal reflexes were absent, the deep reflexes equal and hyperactive. There was no Babinski sign and no clonus. There were leukorrheal discharge, a lacerated cervix and pelvic exudate on the right. The blood count was normal, and the blood pressure was: systolic, 120; diastolic, 80. The Ewald test showed absence of free hydrochloric acid.

Course of Illness.—The patient was sent home, improved, and readmitted five days later, October 11. Persistent vomiting had recurred with severe

continuous sticking pains in both thighs. Weakness in both lower extremities was so marked that she could not stand without assistance.

Physical Examination on Readmission.—Examination revealed: paresis of both lower extremities, absence of knee and ankle reflexes, marked hyperesthesia over both legs, but no loss of sensation.

Course of Illness.—Three days after readmission, she had a general convulsion; there was no rise of temperature. The blood count and urine were normal. The spinal fluid was clear—four lymphocytes per cubic millimeter.

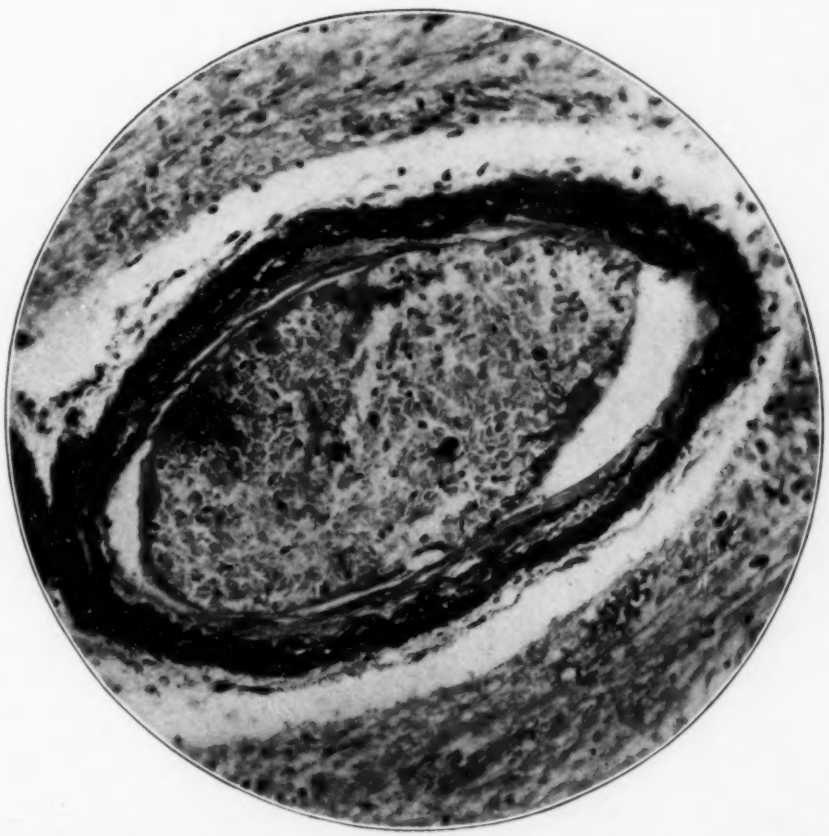

Fig. 6.—Lenticular nucleus; medium sized vessel showing the accumulation of a lipoid substance in its adventitia and media.

On October 18 paresis of both external recti was noted, nystagmus similar to that obtained on stimulation of the semicircular canal and marked engorgement of the vessels in both disks. Blood count: 18,000 white cells, polymorphonuclears 80 per cent. On October 19 paresis of the external recti became more marked, chiefly on the right. The right palpebral fissure had become wider. Hyperesthesia in both lower extremities persisted. The patient complained of severe pains. Knee and ankle reflexes were absent. Vomiting was less intense. Beginning choked disk was noticed. The muscles of the legs were

tender. There was no Babinski sign and no atrophy. Hearing was normal. From this day until October 24 there was slight improvement. The vomiting had stopped. Paresis of the eye muscles had become less. On this date the nystagmus increased. The patient choked on taking fluids; she had difficulty in clearing her throat of mucus. There was paresis of the palate; speech was nasal. Tenderness in the legs had increased. The pulse was very rapid. Death occurred on October 25 from respiratory paralysis. The temperature rose to 100.4 F. a few days before death. At the time of death it was 102.2 F. The urine showed a faint trace of albumin.

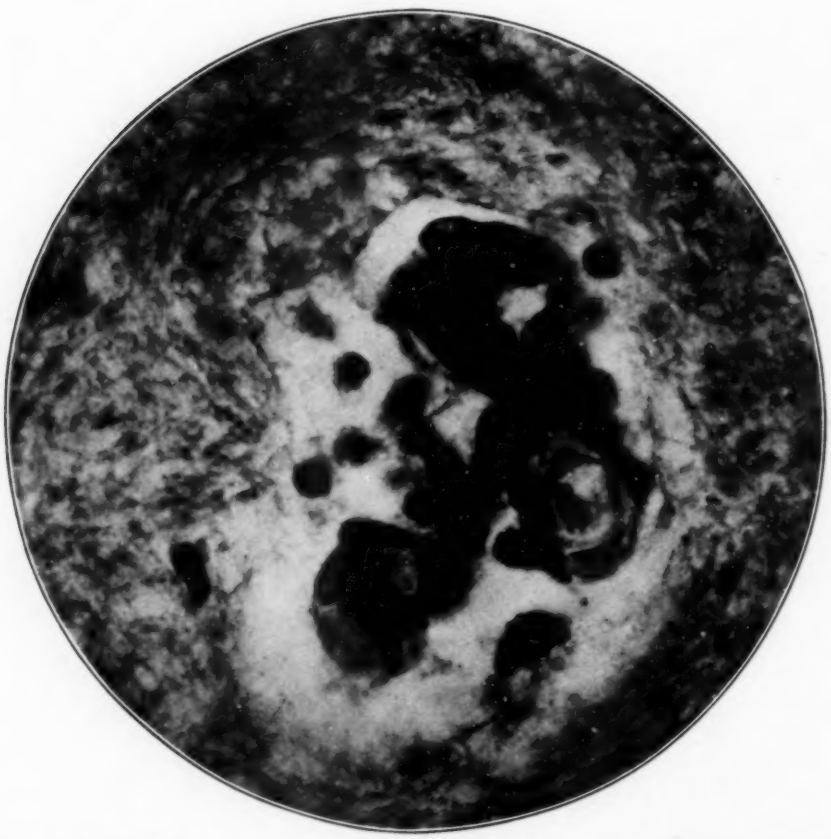

Fig. 7.—Three small capillaries showing swollen endothelial lining; adventitia thickened and surrounded by a small number of gliogenous, granular cells.

COMMENT

Subacute encephalitis has certain common clinical characteristics. There are two groups. In one the onset is acute with the clinical picture of that stage. In the other, the onset is insidious and the nature of the infection often is not recognized. In these cases there is a history of headache, malaise, dizziness and weakness; occasionally blurred vision, rarely transient diplopia; frequently a history of catarrhal inflammation

of the upper respiratory tract. This condition may last for weeks without being regarded as of serious moment. In both groups there follows a stationary period or one of improvement for a variable length of time. In the last stage there is rapid development of serious symptoms referable to extensive involvement of the midbrain and the medulla, with rise of temperature, generally a rapid pulse and fatal outcome from respiratory paralysis.

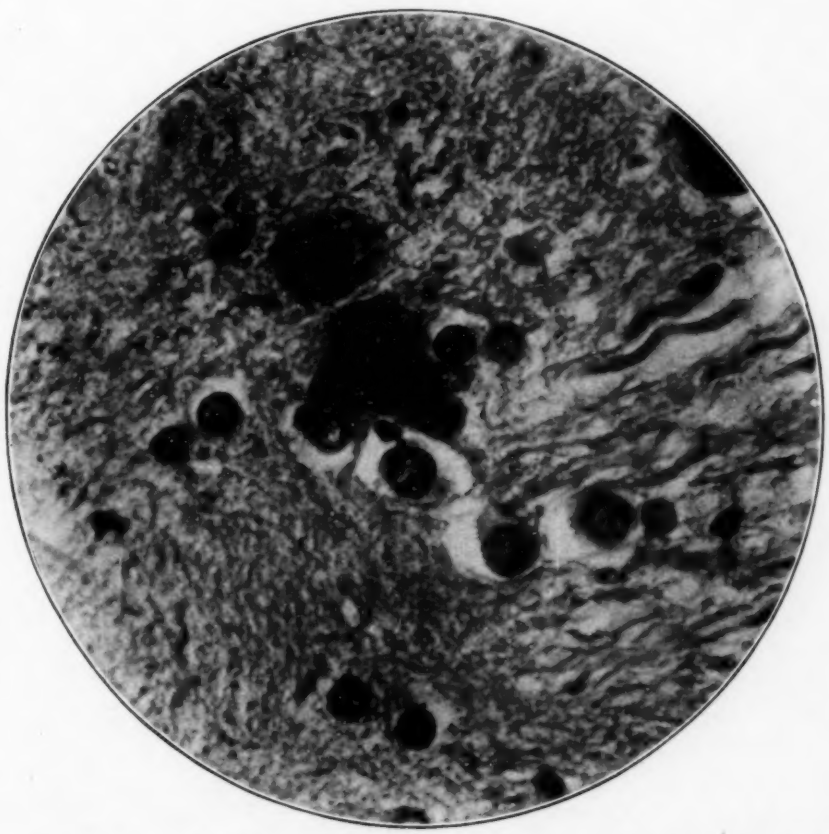

Fig. 8.—Area of glial-proliferation. Glial cells are seen here with mitotic figures.

PATHOLOGIC ANATOMY

We present herewith results of examination of the brain of each of the cases reported above. Particular attention was paid to the midbrain, basal ganglions, the region of the dentate nucleus in the cerebellum, and the medulla oblongata. The spinal cords were not available and in only one case were the thoracic and abdominal viscera examined. Formaldehyde solution, Weigert's glia mordant, and Zenker's fluid were employed for fixation. Celloidin paraffin and frozen sections

were prepared. Delafield and Heidenhain's hematoxylin, Bielschowsky's silver stain, van Gieson's resorcin fuchsin, Spielmeyer's myelin stain and Herxheimer's fat stain were used.

Gross Anatomy.—The dura in all cases was normal. The pia-arachnoid was smooth, glistening, somewhat edematous, but extremely congested. The congestion imparted to the surface of the brain a deep purple hue, most marked on the ventral surface of the pons and medulla. There were no subpial or sub-

Fig. 9.—Ganglion cells from the floor of the aqueduct of Sylvius. Note the enormous amount of fat displacing the nucleus, and giving it the appearance of a giant fat cell (Camera Lucida drawing).

arachnoid hemorrhages. In Case 3 there were two small areas of thickening in the pia-arachnoid, one at the occipital pole, the other on the ventral surface of the left cerebral peduncle. The vessels at the base showed no atheroma and their small branches were patent and unchanged. No gross areas of softening were found. Small areas of reduced consistency and darkened color were

found surrounding medium sized vessels, believed to be a beginning process of softening. Engorgement of blood vessels throughout the brain was striking, most prominent in the medulla and pons, the region of the dentate nucleus and around the aqueduct of Sylvius.

Microscopic Anatomy.—A limited number of small and medium sized blood vessels enveloped by fairly thick mantles of lymphocytic infiltration were found (Fig. 1). This infiltration was fairly definitely limited to the Virchow-Robin space (true adventitial infiltration), a condition invariably found in acute epidemic encephalitis.

Fig. 10.—Midbrain, cerebral peduncle. Perivascular hemorrhage; also found in the midbrain and basal ganglions, but not to the same extent as in the medulla. Note the poor staining quality of the vessel coat.

The dominant type of cell in this infiltration was the small lymphocyte, but large mononuclear leukocytes, so-called endothelial leukocytes, polyblasts and a few granular cells, were also present. The granular cells were identified in frozen sections by fat stains. Fat granules, however, were not limited to these granular cells, but were also present in the endothelial cells of the blood vessels, suggesting a phagocytic function of these cells. Vessels showing this adventitial infiltration appeared to be limited to certain zones, such as those about

the aqueduct of Sylvius, the inferior olive, and the dentate nucleus. It is rather significant that they should be found in limited numbers and be restricted to the parts that were affected early, if not first, by the disease.

A widespread and more obvious alteration of the structure of the mesodermal elements was found in the productive changes in the adventitial coats of the blood vessels. Throughout the brain stem, vessels, though variable in number and in intensity of reaction, presented a striking thickening of the adventitial coat. Apparently this thickening was brought about by proliferative changes in the adventitia; polyblasts and recently formed fibroblasts were found in abundance and apparently had led to the organization of fibrous tissue in the wall of the vessel. Various stages in the development of fibroblasts and resultant mature fibrous tissue were observed. There were vessels in which polyblasts were most numerous, with only a few fibroblasts (Fig. 2); also vessels in which young fibroblasts predominated; and, finally, there were vessels in which the polyblasts and fibroblasts were completely replaced by mature connective tissue (Fig. 3). These changes almost completely overshadowed the infiltrative reactions and should be regarded as the sequel of the latter.

The formation of new blood vessels is another feature of no less importance. Groups of small, recently formed, already patent capillaries existed in all parts of the brain stem (Fig. 4). Rod cells (Stäbchen) were present in large numbers all through the brain, but especially in the regions with many new capillaries. In several instances such cells were found branching out from adventitia (Fig. 2). In medium sized vessels the endothelial cells frequently were swollen and increased in number (Fig. 5). In Case 1, medium sized vessels in the region of the dentate nucleus and in the lenticular nucleus showed in the intima and adventitia accumulations of lipoid substance resembling arteriosclerotic plaques (Fig. 6). In Case 3, in which arteriosclerosis is ruled out by the age of the patient, the same changes in the same region were present. Furthermore, special stains failed to show any change in the elastic membrane.

The glia changes were mainly mild forms of proliferation and mobilization of glial elements about blood vessels and in the subependymal layer of the floor of the fourth ventricle and of the aqueduct of Sylvius. These changes were seen near small arterioles and capillaries (Fig. 7). There were small accumulations of glia cells in groups of five to eight about ganglion cells undergoing neuronophagia, but this grouping frequently bore no relationship to degenerating ganglion cells. Economo's view that they represent landmarks of ganglion cells undergoing phagocytosis is probably correct. These changes were limited to the brain stem and basal ganglions.

"Gitter" cells, probably glial in origin, were found in fairly large numbers in proximity to medium sized blood vessels, in areas which we had noted in the macroscopic examination as being probably areas of beginning softening. The myelin sheaths of nerve fibers in these areas were swollen, and there was some fragmentation. There was also evidence of active glial proliferation. Numerous mitotic figures were present (Fig. 8). The form of glia cells developed was of the ameboid type; no monster fiber forming glia cells were found.

Evidence of an extensive degenerative process in the ganglion cells was shown in chromatolysis, displacement of the nucleus, neuronophagia and abnormal quantities of fat-staining bodies. The last were often in such masses as to displace the nucleus and produce the appearance of a giant fat cell (Fig. 9). These changes were most marked in the basal ganglions, the midbrain and

medulla, and were found to a lesser degree in the cerebral cortex. This process led to accumulation of large quantities of fat in the adventitial spaces of the neighboring blood vessels.

Perivascular and extravascular hemorrhages (Fig. 10) were numerous in the medulla, pons and midbrain. That these hemorrhages were not agonal is shown by the presence of blood pigment in the adventitial spaces in parts of the brain remote from the seat of the extravasation of blood. It is also noteworthy in its bearing on the clinical course of the disease that the hemorrhages were most extensive and most frequent in the medulla oblongata. Another noteworthy point is that wherever hemorrhages occurred the walls of the vessels showed no thickening or perivascular infiltration. Apparently these vessels were spared in the first phases of the disease, and during its exacerbation the adventitia was damaged to such an extent that it was incapable of proliferative changes and could not withstand the pressure of the vascular engorgement. Such changes were rarely found in other parts of the brain.

SUMMARY

The lesions of the small vessels form an uncommon and most prominent feature in these cases. With the findings in six cases of the acute form of lethargic encephalitis, they lead us to believe that the primary attack of the virus is on the small and medium sized vessels, and that these are affected to a degree proportionate to the virulence of the virus.

It appears to us that the production of elements of infiltration, destined perhaps to repair damage occurring in the immediate vicinity of the vessel, is an important function of the adventitia. Thus, when a virus or even a mineral poison (Hassin [3]) reaches the adventitia, it reacts by formation of adventitial elements, provided that the vessel wall is not damaged to the extent of losing its potency for further proliferation. Should the virus or toxin be so destructive to the vessel wall as to incapacitate it for cell proliferation and weaken it so that it cannot withstand the pressure of vascular engorgement, perivascular hemorrhages would occur in large numbers, as happens in the acute, virulent type of the disease. When the virus reaches the vessel in a small amount or in attenuated form, changes pointing to subacute lesions follow, as was shown in our cases.

Such interpretation of the histologic changes leads us to suggest the following division of epidemic encephalitis:

1. An acute infiltrative form, the dominant feature being perivascular infiltration.

2. An acute hemorrhagic form, in which the virulence of the disease is indicated by numerous extensive hemorrhages.

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3. Hassin, G. B.: Histopathologic Findings in a Case of Superior and Inferior Poliencephalitis with Remarks on the Cerebrospinal Fluid, Arch. Neurol. & Psychiat. **5**:552 (May) 1921.

3. A subacute productive form, as described in this paper.

The acute infiltrative form is the early state of any acute form of epidemic encephalitis, which may pass into the fatal hemorrhagic type or the protracted, mild productive form.

The anatomic changes in these cases afford sufficient basis for the hypothesis that the sequellae which frequently follow an attack of acute epidemic encephalitis are due mainly to vascular changes with consequent gliosis and degenerative changes in the parenchyma. Thus, it is not improbable that in various post-encephalitic conditions of a progressive character (E. J. Parkinson type), there may be a more or less localized lesion, characterized by progressive changes in the adventitia and intima of the cerebral vessels, accompanied by gliosis and secondary parenchymal degeneration, directly responsible for the clinical manifestations.

THE CRANIAL HYPEROSTOSES PRODUCED BY MENINGEAL ENDOTHELIOMAS*

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BOSTON

This communication will be chiefly devoted to but one of the many interesting features of the endotheliomas, namely, the hyperplasia of the adjacent bone. That the relationship between the meningeal tumor and the hyperostosis is not generally understood was brought out at a recent meeting of the Society of Neurological Surgeons held in Philadelphia. At that time Professor Spiller exhibited many interesting specimens from his extensive collection of brain tumors. In showing some examples of endotheliomas he stated that these tumors were sometimes associated with an overlying cranial hyperostosis which he considered to be the cause of the subjacent growth. This opinion was so contrary to that which has long been held and taught in the writer's clinic, that this occasion is taken to present some data bearing on this particular aspect of these lesions.

It is quite probable that the true character of the bony tumor has often been overlooked because the necessity of decalcification has deterred observers from making a careful histologic study of the adjacent portion of the skull as well as of the tumor proper. This, I must admit, applies to some of the early examples of hyperostosis cranei accompanying endotheliomas in my Johns Hopkins series. My attention was first drawn to the true nature of the bony tumor by an experience which may be briefly stated.

The patient came under my care in February, 1910, giving the following history: Twelve years before he had received a sharp blow on the vertex of the head approximately at the rolandic point. This point remained somewhat tender, and in the course of time a local prominence of the skull, attributed to an epicranial exostosis, became apparent. Occasional attacks of focal epilepsy involving the left foot and leg subsequently occurred, and under the assumption that these attacks were produced by cortical irritation, a surgeon in 1905 trephined and removed the small area of thickened bone. The underlying dura which was exposed was thought to be normal, and the membrane was not opened. The thickened disk of bone which had been removed showed tumor on microscopic examination. It was classified by a pathologist as a primary psammosarcoma of the diploe.

For the next five years the patient's jacksonian attacks continued unabated, with increasing disability and spasticity of the affected foot. There was no local recurrence of the tumor at the site of the bone defect, and in the absence

* From the Surgical Clinic of the Peter Bent Brigham Hospital.

of the usual manifestations of pressure (headache, choked disk, etc.) an intracranial tumor was not suspected by any of the several neurologists and surgeons who were subsequently consulted.

By the time of his admission to the hospital in 1910 the left arm had begun to be involved in the spasticity and an osteoplastic exploration was decided on. This disclosed a large potato-like psammo-endothelioma which had greatly deformed the right hemisphere. The tumor, which weighed 198 gm., was successfully enucleated. Its meningeal attachment was situated alongside the sinus sagittalis, directly under the small bone defect made at the original operation.

Though the dural attachment of the tumor at the sinus was not removed and was unquestionably infiltrated by tumor, there has been no evidence of continued growth though twelve years have elapsed.

Since this experience, areas of cranial thickening, whether disclosed by palpation or by roentgen ray, have always been looked on with the suspicion that they might overlie a meningeal endothelioma. It, however, was not appreciated for some time that these tumors in their intradural aspects might be of two distinct types: (1) *massive tumors* with a relatively small area of meningeal attachment, and (2) *tumors en plaque* which are but slightly elevated though they may involve a considerable area of dura. Though the former may in a certain percentage of the cases be accompanied by an overlying hyperostosis, the bony thickening is apt to be much more pronounced in the case of the flat tumors. As a matter of fact, were it not for the hyperostosis and its consequences, many of these meningeal tumors would pass unrecognized, for they may give no intracranial symptoms of tumor either general or localizing. Indeed, the massive, potato-like endotheliomas may sometimes attain very large dimensions before general pressure symptoms, such as choked disk or headaches, are manifested. This was true of the patient with the 198-gram tumor whose case has just been mentioned.

The endotheliomas have their definite seats of predilection, a full discussion of which must await a subsequent and more extensive report. It will suffice, for the present, to say that the tumors which are parasagittal in origin, and those which arise from the temporofrontal meninges adjacent to the sylvian cleft seem to be accompanied by a hyperostosis cranei more often than those in other situations.

For purposes of this report, a single comparatively recent example of one of these temporal lesions has been chosen. The region is one in which endotheliomas frequently arise, and when they are associated with marked hyperostosis, as in this particular case, exophthalmos is almost invariably produced.

REPORT OF A CASE

Left temporosphenoidal endothelioma en plaque, with invasion and thickening of overlying bone and extracranial involvement of temporal muscle.

April 18, 1921.—Admission of Mrs. Mary D., aged 39, referred by Dr. Byrnes of Springfield, Mass., with a bony tumor of the orbit, producing exophthalmos.

Past History.—No apparent bearing on present trouble. Excellent general health. No recorded trauma. Occasional headaches since childhood; none for past year. Married at 27 years; six pregnancies with only two children surviving. Four of them were stillborn at seven months: attributed to renal complications. Last pregnancy was terminated June, 1920, because of eclampsia and convulsions: placenta praevia.

Present Complaint.—For possibly ten years the left eye has been somewhat more prominent than the other. No significance was attached to this, even when in September of 1919 the eyelids on this side became somewhat edematous. As she had some albuminuria and her ankles were apt to be swollen, the puffiness of the eyelids, though unilateral and persistent, was discounted. In Febru-

Fig. 1.—Appearance on admission, showing exophthalmos. The bony protrusion is evident, though partly concealed by her hair.

ary, 1920, she first observed a swelling in the anterior part of the left temporal fossa. It was painless, hard, not sensitive to pressure. Her physician at the time evidently regarded the condition as syphilitic and prescribed the usual drugs, but she did not persist in their use.

On the termination of her pregnancy in June she first noticed some slight loss of visual acuity in the left eye.

For the next six months there was a slow but steady enlargement of the aforementioned bony tumor of the temporal fossa, accompanied by an increasing prominence of the eye and edema of the lids. For the three months before admission the symptoms had developed more rapidly.

Physical Examination.—This was essentially negative except for the obvious local lesion, namely, a smooth, hard tumor, slightly tender on pressure, filling out the left temporal fossa and obliterating such bony landmarks as the external

angular process and zygoma. Associated with the growth was a moderate unilateral exophthalmos with edema of the eyelids (Fig. 1). The exophthalmos was without bruit or pulsation, though over the bony tumor the extracranial vessels were noticeably dilated. The patient was markedly myopic and a slight hyperemia, particularly of the left optic disk, was present. The visual fields were normal. There was slight weakness of the left abducens.

The situation of the growth was obscurely shown in a series of stereoscopic roentgen-ray plates. These (Fig. 2) indicated an area of increased density in the region of the squamous wing of the temporal bone, the sphenoid, and left side of the orbit.

Fig. 2.—Lateral roentgenogram of sellar region showing area of increased density.

The neurologic examination was negative in all respects. The Wassermann reaction was negative. Urine showed a trace of albumin, but functional renal tests revealed no such degree of dysfunction as to contraindicate operation.

May 4, 1921: Operation. Extirpation of hyperostosis together with underlying dura and its subjacent flat tumor.—A curvilinear incision (Fig. 4) was made with its base between the external angular process and the tragus. On reflecting the scalp and temporal muscle so as to expose the bony lesion, it was found that the lower layer of muscle fibers were infiltrated by tumor over the most prominent part of the bony protuberance. The skull at this point was

considerably roughened, and the muscle was adherent to it. This small area of obvious involvement of extracranial tissues was excised and an immediate frozen section showed endothelioma.

The area of hyperostosis, which was difficult of access, was then attacked by making a circle of perforations at its periphery. These perforations, made by using a succession of motor-driven burrs of graduated size, were carried down through the dense bone to the dura. It would probably have been easier to have "burred" away the entire hyperostosis in this fashion, but it was desired to preserve an intact portion of the thickened bone for subsequent study.

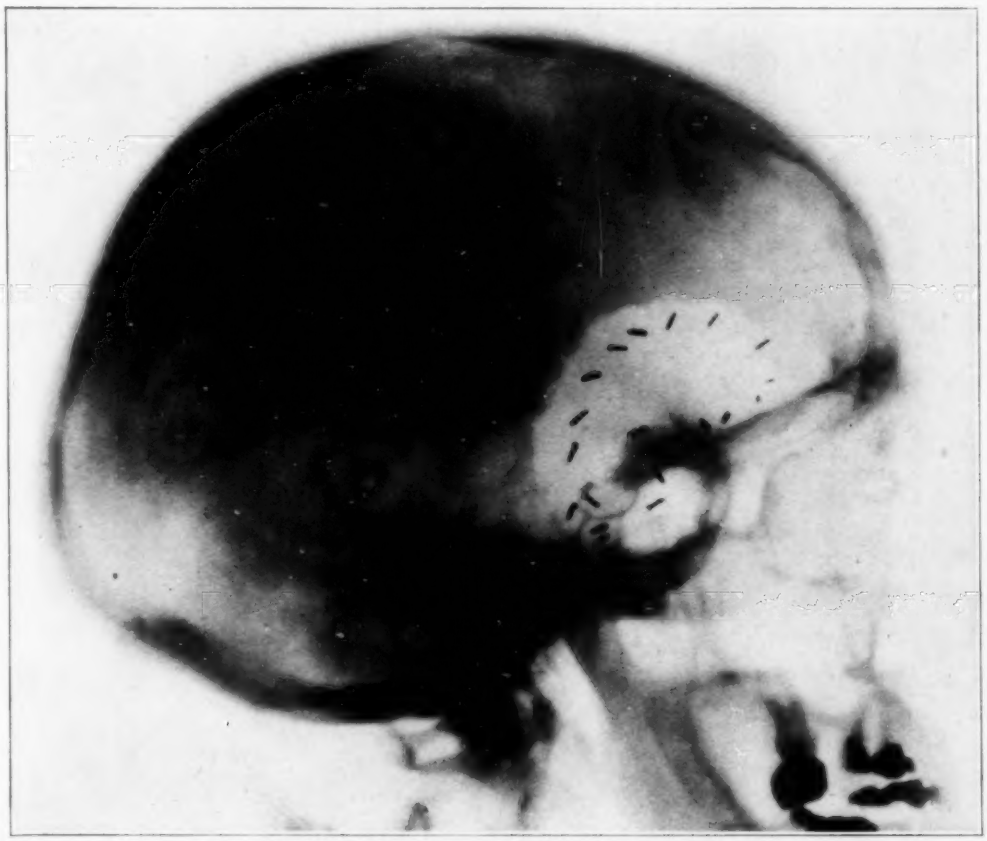


Fig. 3.—Print of postoperative radiogram showing extent of bony removal and situation of clips outlining area of excised dura.

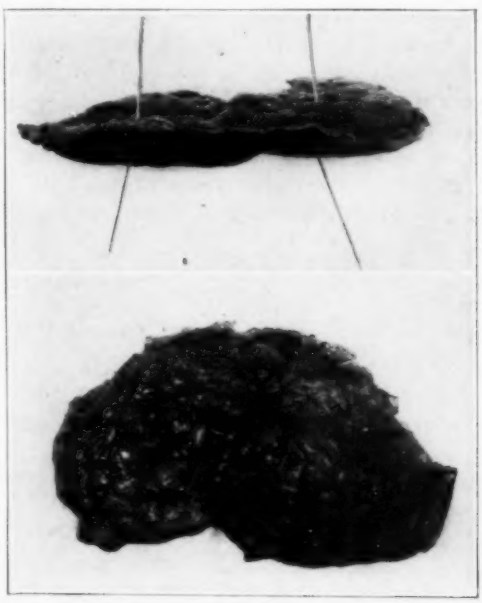
The chief difficulty lay in the complete removal of the hyperostosis at its anterior and lower periphery. In this situation it was necessary to carry the perforations obliquely through solid bone which proved to be 3 to 4 cm. in thickness, before the orbital cavity was reached. The remaining central and posterior mass of bone (Figs. 9-11) was then broken out in a single piece. With the view thus given it was possible, with the further use of burrs and rongeurs, to enlarge the opening until all the thickened bone so far as could be told, was removed. In this procedure the entire outer side of the orbital contents, which had evidently been considerably encroached on by the growth,

Fig. 4.—Twelve days after operation, to show the field and situation of the curved incision, its limits indicated by crosses.

Fig. 5.—Condition ten months after operation (for comparison with Fig. 1).

was fully exposed. Removal of the sphenoid wing was carried inward to the region of the left anterior clinoids in the depths of the sylvian groove.

At the bottom of the bone defect thus made, roughened dura was exposed covering practically the entire tip of the temporal lobe. There was no certainty as to what underlay this thickened dura, whether an endothelioma of the plaque variety or a rounded tumor. The membrane was opened at the upper margin of the bone defect where it was evidently normal in appearance and the edge of a flat endothelioma was seen. The incision in the membrane was then carried around between normal dura and the edge of the tumor, giving the latter a free margin of a few millimeters.



Figs. 6 and 7.—Photographs (natural size though considerably shrunken by fixation) of major portion of tumor; seen on edge in upper figure and from the inner dural surface in the lower figure.

It is quite possible that at the very depth of the sylvian cleft where the field became somewhat inaccessible, some portion of the involved bone and dura may have been left behind.

The dura was so vascular that silver clips were placed on its margins for purposes of hemostosis as the incision to outline the growth was being made. The situation and extent of the flat tumor is consequently well shown in the roentgen-ray picture subsequently taken (Fig. 3).

The operation, though a prólonged one, was well borne. Convalescence was uneventful (Fig. 4), and at the time of her discharge the exophthalmos and edema of the orbit had largely disappeared.

At the present writing, ten months later, she remains free from symptoms; there is no indication of any tumor growth from the possible remaining fragment; the exophthalmos has almost completely subsided (Fig. 5).

Pathologic Report.—The three chief fragments of tissue saved for study consisted of: (1) the primary tumor adherent to the under surface of the dura; (2) a portion of the thickened overlying skull; (3) a fragment of the temporal muscle.

1. *The tumor proper.* There are two fragments. The larger (Figs. 6 and 7) shows a flat growth with nodular surface, springing from the under side of a semicircular piece of dura measuring 5 by 3.5 cm. in diameter. A margin of free dura surrounds the growth except at one portion of the specimen where the tumor has been cut into. At its thickest place the growth is only about 4 mm. in thickness. On section it shows a typical endothelioma which is plastered on the inner surface of the membrane, the cell masses being arranged in fibrous alveoli (Fig. 8).

2. *The bone fragment.* (Figs. 9-11.) This is a wedge-shaped piece of bone measuring 5 by 3 cm. in its surface diameters, and nearly 3 cm. in its greatest thickness. The outer surface is roughened and irregularly grooved, and some fragments of muscle adhere to it. The inner surface, likewise, is rough and grooved, with fragments of firmly adherent dura. The third surface shows a cup of smooth eburnated bone evidently made by a large burr. A histologic study of the bone showed that its canals are everywhere invaded by tumor (Fig. 12).

3. *The fragments of muscle* removed early in the operation show on section (Fig. 13) invasion with tumor cells arranged in characteristic endothelial alveoli.

Dr. Victor Jacobson's pathologic note regarding the hyperostosis reads as follows:

"The bone is of cancellous type with the marrow spaces containing large groups of spindle cells arranged in the whorl-manner of dural endothelioma and similar to the tumor in the muscle described. The bone is dense and arranged in trabeculae. The resulting spaces contain the tumor cells which are surrounded by a thin compact layer of fibroblasts which in turn are separated from the bony trabeculae by loose connective tissue in which are a few thin-walled blood vessels. There is no apparent intravascular growth of tumor but the tumor cells have gained access to the marrow spaces and grown in them, often compressing the marrow vessels but not penetrating them. In one marrow space active hematopoiesis is in progress."

INCIDENCE

At the present writing (Jan. 1, 1922), in a series of considerably over one thousand presumptive cases of tumor, the lesion has been verified in 748 instances.[1] Without going into the detail, unnecessary for our present purposes, of distinguishing between the various subvarieties of gliomas, adenomas and so on, these cases may be tabulated

1. The significance of the term "verified" and the way in which the brain tumor cases in the clinic are classified as *verified, non-verified and tumor-suspects* has been made clear in recent papers by Percival Bailey (Concerning the Clinical Classification of Intracranial Tumors, Arch. Neurol. & Psychiat. **5**:418-437 [April] 1921) and by C. E. Locke (A Review of a Year's Series of Intracranial Tumors, Arch. Surg. **3**:560-581 [Nov.] 1921).

as follows, in order to indicate the ratio of the endotheliomas to other main tumor groups:

	Number of Cases	Percentage
Glioma	312	41.7
Adenoma (chiefly pituitary)	174	23.2
Endothelioma	80	10.7
Neurinoma (acoustic)	60	8.0
Congenital tumors	40	5.3
(a) Suprasellar tumors (chiefly of pharyngeal pouch origin 34		
(b) Cholesteatomas and dermoids 6		
Granuloma	34	4.5
(a) Gumma 13		
(b) Tubercle 21		
Papilloma (choroid plexus)	8	1.1
Angioma	6	0.8
Metastatic and invasive	24	3.2
Unclassified	10	1.4
	748	

Thus, of the brain tumors encountered and histologically verified in this personal series, the endotheliomas represent 10.7 per cent. and occur in the ratio of one to four of the gliomas.[2]

HYPEROSTOSIS CRANEI

Of the eighty endotheliomas, twenty were accompanied by a recognizable thickening of the overlying bone. For reasons not as yet entirely clear, endotheliomas *en plaque* are more likely to provoke bony thickening from tumor invasion than are the large rounded tumors. Leaving out of consideration a few of the spreading endotheliomas of the basal meninges, such as those which arise from the gasserian envelops,[3] nearly all of the flat tumors of the type recorded in the foregoing case report have produced an overlying hyperostosis. There have been eight of them in all, five in the anterior temporal region, as in the case recorded, usually with unilateral exophthalmos, and three in the parasagittal region of the vault.

The other twelve examples of hyperostosis have accompanied the rounded tumors which cause marked cerebral deformation. It was my early impression that these tumors were less likely to invade the bone because of their relatively small area of meningeal attachment. However, this cannot be the actual explanation, for the reason that there are several cases in the series in which a pronounced hyperostosis overlay an enucleable spherical endothelioma which proved to have a comparatively small area of meningeal attachment.

2. In his recent article on "The Accomplishments of Intracranial Surgery" (New York State J. M. **21**:369, 1921), Dr. Frazier has made the statement that 60 per cent. of his cases were sarco-endotheliomas and only 38 per cent. gliomas.

3. Reference has already been made in another connection to the four endotheliomas in my series which have apparently arisen from the trigeminal sheath. "The Major Trigeminal Neuralgias," Am. J. M. Sc. **109**:157, 1920.

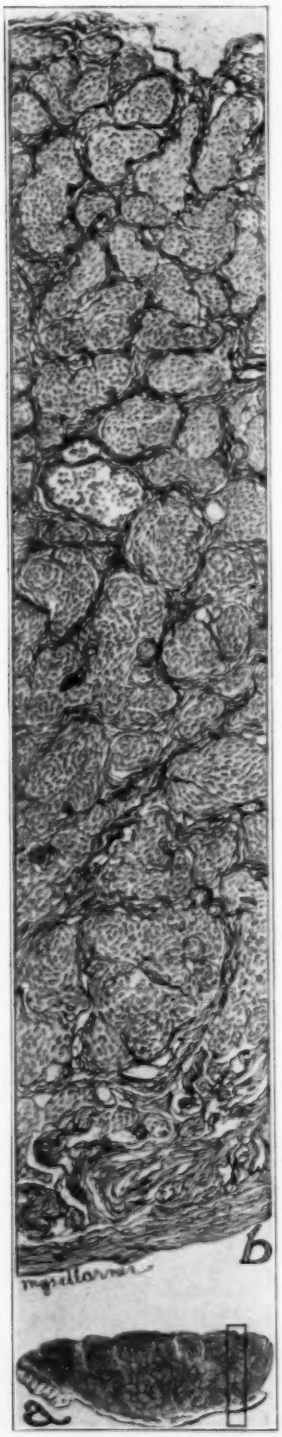


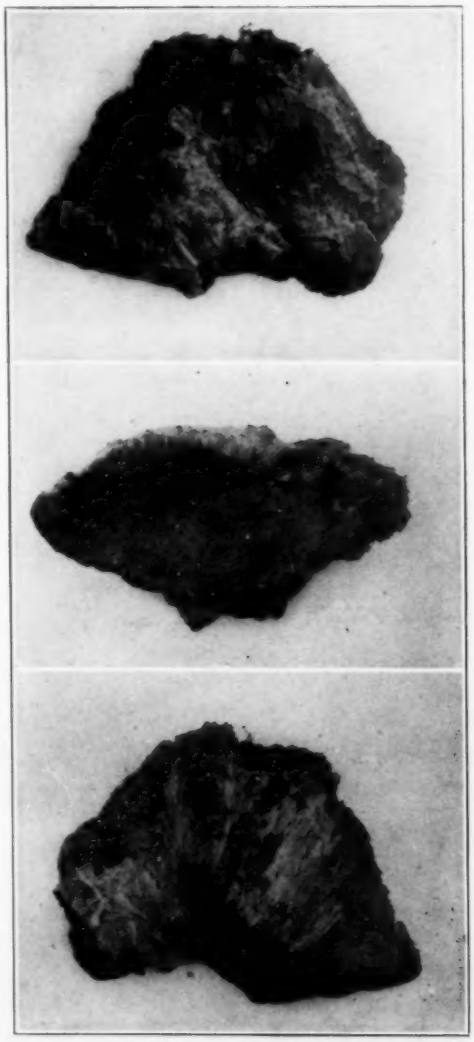
Fig. 8.—Microscopic low-power drawing through entire thickness of tumor.

The endotheliomas must be regarded of course as benign tumors, but it is known that the growth tends to insinuate itself into crevices and may surround and incorporate important anatomic structures like the blood-vessels of the cranial base without damaging them.[4] In view of this it might be assumed that under the influence of intracranial tension the tumor cells in the process of their multiplication become crowded into and through the vascular dural spaces and finally into the canaliculi of the bone. In consequence of this the bone becomes irritated, with subsequent osteoblastic proliferation which provokes the hyperostosis. There can be little doubt that the thickening occurs in this way, but intracranial tension can have nothing to do with it, in view of the fact that the flat endotheliomas which do not increase tension are, as we have seen, those which most often tend to invade the bone. There must be some other reason, therefore, to account for this peculiar process. One occasionally finds a meningeal endothelioma in which there is a tendency to bone formation within the tumor itself, and therefore the process may bear some relation to the bone-forming properties of the meninges, but without further data on the subject speculation is futile.[5]

4. In another connection (with C. B. Walker) an example has been given of a basal endothelioma which had extruded itself far into the vaginal sheath of both optic nerves without destroying the tissue relationships. This case, one of the typical tumors arising from the olfactory groove, an example of which was pictured by Cruveilhier, was first reported in my monograph "The Pituitary Body and Its Disorders," Philadelphia, W. B. Saunders Co., 1912, and later on from its ophthalmological aspects with C. B. Walker: Arch. Ophth. **45**:427 (Sept.) 1916, p. 427.

5. In an article with Lewis H. Weed (*loc cit.*) we described and figured one of the endotheliomas of this series in which there were deposits of true bone, not only in the tumor but also in the arachnoid elsewhere.

The twenty examples of hyperostosis in the series of eighty endotheliomas represent one in four, but unquestionably this is too small a percentage if one takes into consideration the cases in which a slight thickening is observed on the inner surface of the skull alone. In most



Figs. 9, 10 and 11.—Three views (natural size) of bone fragment, showing its outer surface in the upper figure, the dural surface in the lower figure, and its thickness in the middle figure. The dark points on the burred surface of the middle figure represent macroscopic evidences of tumor.

of the tumors of spherical type the point of origin of the growth from the meninges is clearly apparent. At this central core of the tumor the dura is apt to be indented by a slight endostosis, often too

small to be recognized by the roentgen ray and in the operative notes of this long series of cases the particular fact may not always have been recorded.

In short, the tumors do not always behave alike in their effect on the bone. In some cases, aside from the increased vascularity with widening of the diploetic venous channels owing to stasis, there is no apparent change. In others, the bone may become greatly thinned

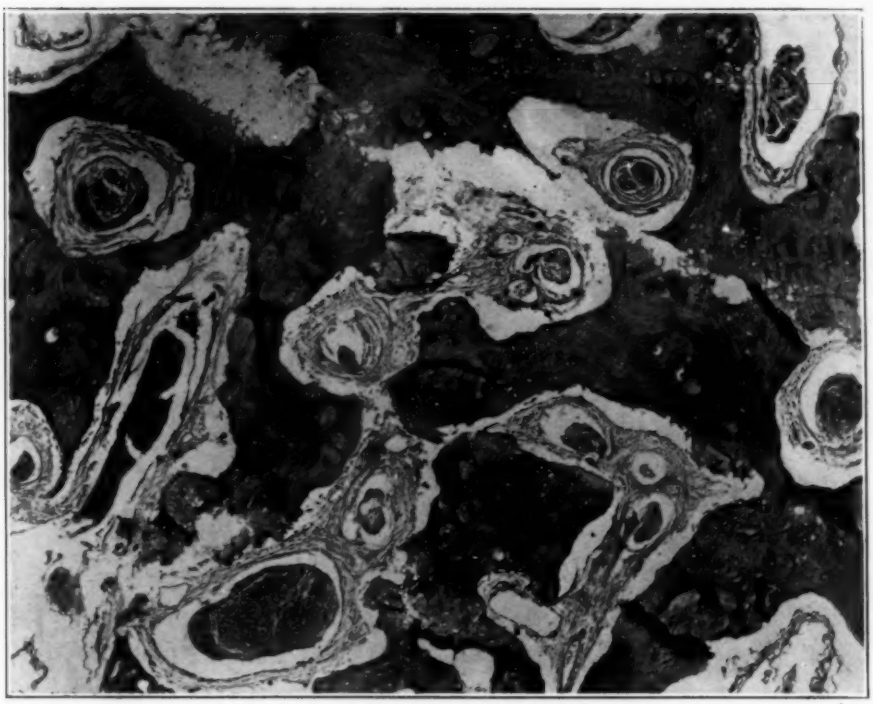


Fig. 12.—Low-power photomicrograph (×60) of section of endothelial hyperostosis.

and the tumor find its way to the surface without any actual tumor penetration of dura. In still other cases, when a marked hyperostosis has been produced, the central portion of the hyperostosis may through subsequent absorption become occupied by tumor cells to the exclusion of anything more than occasional bony spicules, and in these cases the appearance of the bone in the roentgen ray may closely simulate a primary sarcoma of malignant character.

Apart from their relation to the cranial hyperostosis, these tumors have many features of unusual interest. Some of these points have been touched on in other connections. Thus, in a paper with Weed in our series of articles on the cerebrospinal fluid, the fact that they are in all probability of arachnoid rather than dural origin, as commonly

believed, was touched on. It is our belief that they arise from the cell-clusters of the arachnoid villi projecting into the dura.[6]

Cruveilhier's designation of these tumors, which he so well described, as "tumeurs cancéreuses des meninges" means little more to us today than does the "fungous dura matris" of his predecessors; and as the term commonly employed, namely, dural endothelioma, gives the wrong impression of the membrane from which the growth has originated,

Fig. 13.—Section of temporal muscle (× 170) showing extracranial endothelial invasion.

the designation *meningothelioma* or *meningioma* is suggested as a compromise. This at least avoids the objections which the embryologist might raise, for strictly speaking the growths would seem to be properly called mesotheliomas of arachnoid origin.[7]

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6. Cushing, H., and Weed, L. H.: Studies of the Cerebrospinal Fluid and its Pathway. IX. Calcareous and Osseous Deposits in the Arachnoidea, Bull. Johns Hopkins Hosp. **26**:367-372 (Nov.) 1915.

7. There are other varieties of endotheliomas from which these common tumors must be distinguished, such as those of supposedly pial origin which have no dural attachment. These are exceedingly vascular growths, sometimes designated as hemangio-endotheliomas. Another type of tumor which is exceedingly rare in man but more common especially in the horse, is that form of endothelioma which arises from the choroid plexus. These tumors have been classified with the cholesteatomas, though the latter are of dermoid or epidermoid origin and bear no relation to the endotheliomas. With endothelial tumors of these sorts we are not here concerned.

Needless to say, were all these tumors associated with cranial hyperostoses they would be easily recognized and localized. Unfortunately they are not. Hence, in the absence of general pressure as well as of localizing symptoms, they may remain for a long time unrecognized and may ultimately reach such a size that their removal, even when they are accessible, is a most formidable operation. The largest tumor in the series weighed 246 gm., and was attended by extreme circulatory stasis. Even when focal symptoms do appear in the course of time, they may be of false localizing value, as was the case with one of these growths described in another connection.[8]

The meningiomas, if they may be thus called, have certain definite seats of predilection, and for the most part each group, on the basis of its anatomic seat of origin, gives a very definite and characteristic symptomatology. A discussion of these matters must await a more extended report on the subject. It is sufficient for this preliminary note to point out in summary:

1. That, in a series of over 700 verified tumors there have been eighty endotheliomas, their ratio to the gliomas being about one to four.

2. That at least 25 per cent. of the endotheliomas are accompanied by an overlying hyperostosis cranei which is either palpable externally or demonstrable by the roentgen ray. This process is due to invasion of the bony canals by tumor cells, with resultant stimulation of osteoblasts and the production of new bone.

DISCUSSION

DR. WILLIAM G. SPILLER, Philadelphia: In 1899 my attention was first called to the subject Dr. Cushing has discussed, and in that year Dr. Kirkbride and I reported a case of localized bony enlargement of the skull over a meningeal tumor before the Section on General Medicine of the College of Physicians of Philadelphia. I believe this was the first report of a case of this kind in literature. The condition was an endothelioma growing from the cerebral dura with endothelioma cells within the bony enlargement.

In 1903, Brissaud and Lereboullet reported two cases in which they considered the tumor of the brain as secondary to the enlargement of the bone of the skull. In one of these cases there had been an enlargement of the bone since childhood, and it was not until the age of 29 that symptoms of tumor developed. Multiple tumors were found growing from the dura. In 1907, I published a paper in *The Journal of the American Medical Association* containing in full a report of my first case, with the report of another similar case. In this second case the patient was syphilitic, and I believed that syphilis was the cause of the bony growth of the skull. A few other cases were reported before 1907.

It has seemed important to recognize that where there is a localized large bony growth of the skull, tumor is likely to be found beneath or near it

8. Anosmia and Sellar Distortion as Misleading Signs in the Localization of a Cerebral Tumor, J. Nerv. & Ment. Dis. **44**:415-423 (Nov.) 1916.

growing from the dura, and this fact is of great importance as regards operation. In one such case, with this thought in mind, I urged exploratory operation although the symptoms of intracranial tumor were not severe. The man refused operation and at necropsy a tumor growing from the cerebral dura was found.

I should like to ask Dr. Cushing in how many of his cases of meningeal tumor microscopic examination of the bony growth was made, and in what proportion of his cases he found by such microscopic examination tumor cells within the bony enlargement. I am willing to acknowledge that tumor cells may be found within the bony enlargement, and in my first case, reported in 1899, such cells were found, but I have not been convinced that the bony enlargement in these cases is always secondary to the meningeal growth.

The matter is one of great importance. If we may believe that the bony enlargement is primary, we may hope to prevent the development of a meningeal tumor by operation at an early date.

Dr. Charles A. Elsberg, New York: I have seen quite a number of cases with the bony changes of which Dr. Cushing has spoken; in two of the patients I had an experience concerning which I would like to ask Dr. Cushing. The involvement of the bone was so extreme that it would have meant an extensive removal of the cranium. In both I did not remove all the tumor containing bone. These patients have remained well, one for five and one for seven years, without further enlargement of the bone and without any symptoms, and apparently either the tumor in the bone grew very slowly or the bony growth was interfered with after part of the tumor had been removed.

Dr. Archibald Church, Chicago: The lack of symptoms in some of these cases is rather a startling clinical feature. I recall an elderly woman who developed a paraplegia with the symptoms of spinal cord tumor. Incidentally one day, to calm her, I put my hand on her head and felt a large defect in the skull. A little further investigation revealed three openings in her skull, in any one of which a hen's egg might have been placed. These findings were confirmed by a roentgenogram of the skull. She never had had a head symptom nor had she complained about her head. At her death, three of these growths which had produced the large windows of the skull were found and also a somewhat similar growth causing spinal paraplegia.

In other cases affecting the brain and leading to operation, the symptoms had been comparatively insignificant.

Dr. Cushing, in closing: In answer to Dr. Spiller's question, the reason why these conditions have not been fully studied is because there is a good deal of difficulty in sectioning bone; and when there is an obvious tumor, the histologic nature of which can be verified easily without decalcification, the overlying bone has been neglected.

In the preparation of this paper I have gone over all of the old specimens and practically all of them have been sectioned. I confess to a certain amount of hesitation, when the nature of a tumor has been verified, to subject an overburdened department on pathology to the necessity of decalcifying the accompanying fragments of bone. However, tumor has been found in every case examined, and I judge that twenty or thirty have been gone over recently.

Dr. Elsberg's point is one with which I can fully concur. These growths are what Paget calls locally malignant tumors. The cases which I have chosen for the lantern slide demonstration in connection with my paper have been the

sphenotemporal tumors. On one slide half a dozen of them were shown. The bone, under those circumstances, is extensively involved throughout the whole temporal fossa The outer side of the orbit is involved, causing exophthalmos, and it is practically impossible in these circumstances to remove all of the affected bone. It is of course not difficult when the area of bony involvement is less inaccessible.

In reply to Dr. Church's question as to the lack of symptoms, the tumors may be multiple, but that is true also of the neurinomas, that is, the acusticus tumors, and there is a very interesting relation between these tumors and the meningiomas. My tumor series now includes sixty-seven acoustic tumors, all of them unilateral. When these lesions are single, there may be slight manifestations of a Recklinghausen's syndrome—a few fibromas on the skin, for example—but usually that is all. When, however, an acoustic tumor is bilateral, as they sometimes are, it is often accompanied by multiple meningeal tumors of the type under discussion. Dr. Bassoe and others have reported cases of this kind. Hence, there is some relation between tumors of these two types, but it is rare to find the lesions multiple.

HISTOPATHOLOGY OF CEREBRAL CARCINOMA *

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In carcinoma of the brain the parenchyma of the invaded portions appears to be replaced by more or less dense masses of carcinoma cells grouped around distended blood vessels, or it may remain in the form of islets surrounded by strands of cancer tissue. Buchholz,[1] Gallavardin and Varay [2] assert that the brain tissue is not actually destroyed but is merely "pushed aside" by the tumor mass within it ("eingesprengt") without provoking reactive phenomena. They say the glia may show proliferation in the immediate neighborhood of the tumor, but the mesodermic tissues—blood vessels and pia—show no reaction. De Fano [3] also emphasizes the absence of mesodermic reaction in carcinoma produced experimentally by transplantation in the brains of mice and rats. Only in animals "partially immune" did he find plasma cells or lymphocytes and "the nerve elements, the ganglion cells, undergoing atrophy." "Lasting proliferation of neuroglia seems," he says, "to appear only under certain conditions."

The pia is variously described by different authors. Siefert [4] says that the pia is more or less involved in every case, either directly or through propagation along the lymph spaces. Girardi [5] found no pial

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* From the Division of Neurology of the College of Medicine of the University of Illinois and the Pathology Laboratories of the Illinois State Psychopathic Institute and Cook County Hospital.

1. Buchholz: Casuistischer Beitrag zur Kenntnis der Carcinome des Centralnervensystems, Monatschr. f. Psychiat. u. Neurol. **4**:183, 1893.

2. Gallavardin, L., and Varay: Etude sur le cancer secondaire du cerveau, du cervelet et de la moelle, Rev. de méd. **23**:441-561, 1903.

3. DeFano, C.: Intracerebral Transplantation of Malignant New Growths, Folia Neuro-biol. **6**:109, 1912.

4. Siefert, E.: Ueber die multiple Carcinomatose des Centralnervensystems, Arch. f. Psychiat. **36**:720, 1903.

5. Girardi, P.: Ueber Karzinommetastasen im Kleinhirn, Monatschr. f. Psychiat. u. Neurol. **31**:184, 1912.

infiltration and Fischer [6] affirmed its absence even when the cancer came in direct contact with the membrane.

Equally contradictory are the opinions as to the mode of propagation of the tumor cells. Siefert [4] believed that the tumor masses spread from the cortex downward into the depths of the white matter along the course of the pial prolongations. He concluded that propagation is "toward the center"; that is, away from the subarachnoid space. Yet in a spinal cord surrounded, mufflike, by carcinoma he found no cancer cells in the parenchyma or septums of the cord. Bastiaanse [7] is more explicit. In a "primary" carcinoma of the left cerebellar hemisphere, he found numerous "metastases" in the cortex and invasion of the subarachnoid space. He therefore concluded that the carcinoma cells were carried to the brain from the subarachnoid space by the cerebrospinal fluid.

Nowhere have we found any description of the condition of the choroid plexus.

Our knowledge of the histopathology of brain tissue when invaded by carcinoma is in confusion, the few contributions on the subject being contradictory. The reason probably lies in the nature of the material studied. When the growth is far advanced the changes are so marked that their interpretation is almost impossible. Only in exceptionally favorable instances can the evolution of the cancer growth and the accompanying phenomena in the parenchyma, glia and mesodermogenic tissues be followed.

We have had the opportunity to study eight cases of intracranial carcinoma,[8] one being especially instructive because the metastatic nodules were young and not broken down, hence especially suitable for study of the problems mentioned. It has been used as the basis for this work, the findings being compared with those in the other cases. From these studies we believe it possible to establish certain features as common to all cerebral carcinomas.

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6. Fischer, O.: Zur Kenntnis des multiplen metastatischen Carcinoms des Zentralnervensystems, Jahrb. f. Psychiat. **25**:125, 1904.

7. Bastiaanse, B.: Primäres metastasierendes Gehirncarcinom, Ztschr. f. d. ges. Neurol. u. Psychiat. **27**:96, 1915.

8. Two were cases of carcinoma of the meninges and six of the brain proper. One of the former has already been reported (Hassin, G. B.: Histopathology of Carcinoma of the Cerebral Meninges, Arch. Neurol & Psychiat. **1**:705 [June] 1919). The second was furnished by Dr. William Thalhimer of Milwaukee. We are indebted to Dr. Peter Bassoe of Chicago for the opportunity to study four and to the Cook County Hospital for two carcinomas in the brain. All showed metastases; two were carcinomas of the lungs, two of the uterus, one of the pancreas, one of the breast, one of the intestine and one probably of the prostate.

MACROSCOPIC APPEARANCE OF THE TUMORS

The tumors appeared as foci of varying size scattered irregularly through the gray and white substance, sometimes transgressing the pia. They were well defined, loosely attached to the surrounding tissues and extremely soft. The smaller foci were more solid and suitable for frozen section. In one case there was a single metastatic tumor involving the area of the basal ganglions, extending into the third

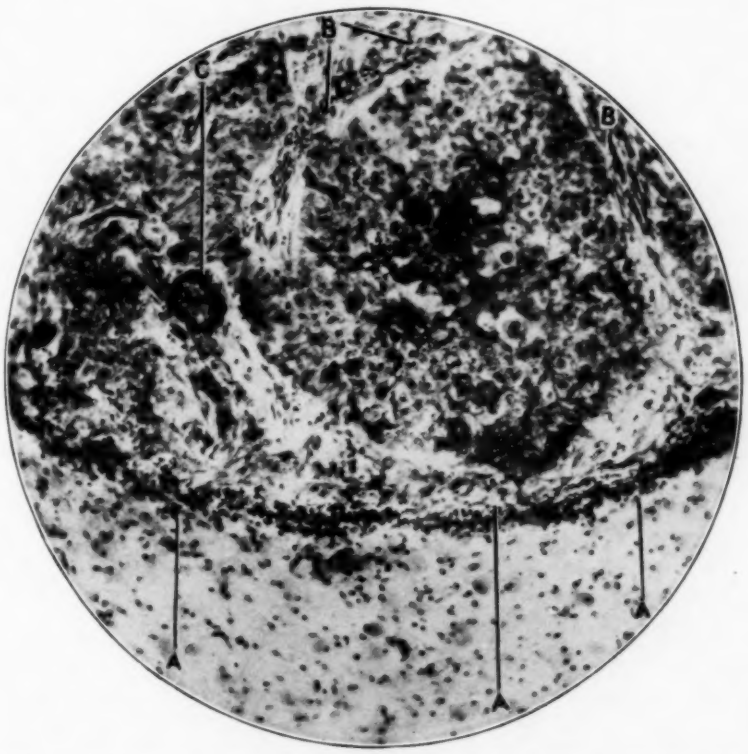

Fig. 1.—Demarcation zone *A,A,A,* dividing the brain below from the cancer foci above; *B,* bands of connective tissue enveloping the larger focus; *C,* a ganglion cell invaded by cancer cells (reproduced under higher power in Figure 3). Thionin; × 125.

ventricle, corpus callosum, cortex and almost reaching but not invading the pia. Here the affected areas were separated from the noncancerous tissue by a well marked zone of demarcation (Fig. 1).

MICROSCOPIC EXAMINATION

The microscopic appearance of the invaded area, the zone of demarcation and the cerebral tissue adjacent to and remote from the

tumor differed from one another. The histology of the carcinoma needs no description; we shall limit attention to the brain tissues.

The Invaded Area.—This presented an areolar appearance with islands of cells separated by bands of connective tissue (Fig. 1). These cells were for the most part ganglion cells in various stages of alteration. The more normal presented a swollen, deeply stained cell body with visible processes and a dislocated nucleus, rich in chromatin. The majority, however, were grossly changed, sometimes to such an extent

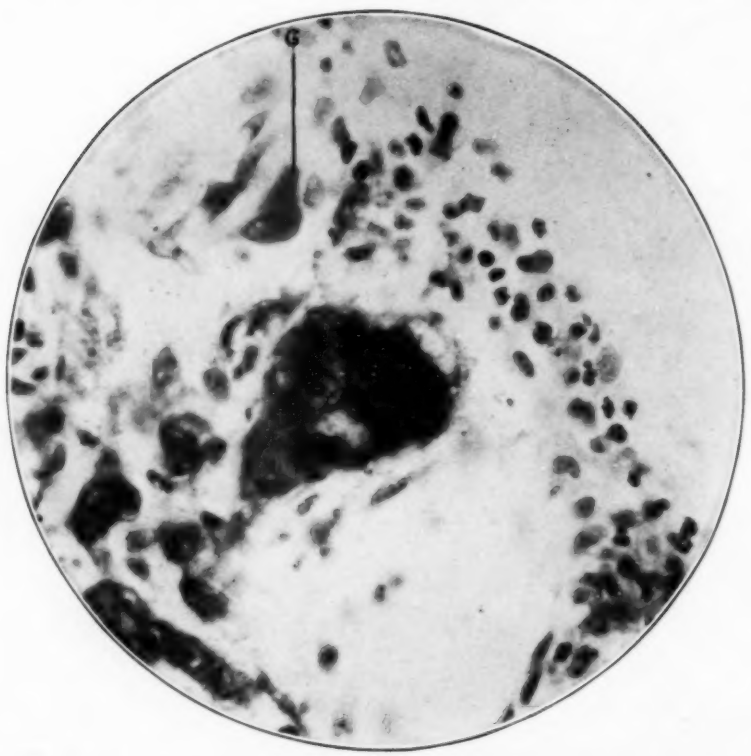

Fig. 2.—The center of the picture is occupied by a ganglion cell, swollen and packed with carcinoma cells, which occupy also the apical dendron. To the left are two smaller ganglion cells also invaded with cancer cells; at *G* a ganglion cell with dislocated nucleus. The elements to the right are lymphocytes, plasma cells, gitter cells and others described in the text. Thionin; × 480.

as to be unrecognizable without further study. As a rule, the cells were large, some truly gigantic (Fig. 2), larger than those to be found in any other central nerve lesion, not excepting amaurotic family idiocy. They were round or irregular in shape, usually pale, some darkly stained, homogeneous or finely granular, devoid of any trace of Nissl's bodies, and the processes were more or less completely obliterated.

The nucleus was swollen, pale and eccentric, the chromatin broken up, but the membrane and nucleolus almost always intact. Sometimes the nucleus stained so faintly that it could be detected only by the presence of the nucleolus. Many of the ganglion cells were vacuolated, others broken up or unevenly stained. With the Bielschowsky silver impregnation some showed a reticulum but, as a rule, the neurofibrils were absent.

The majority of the ganglion cells showed inclusions: granules scattered through the protoplasm, vacuoles containing polymorpho-

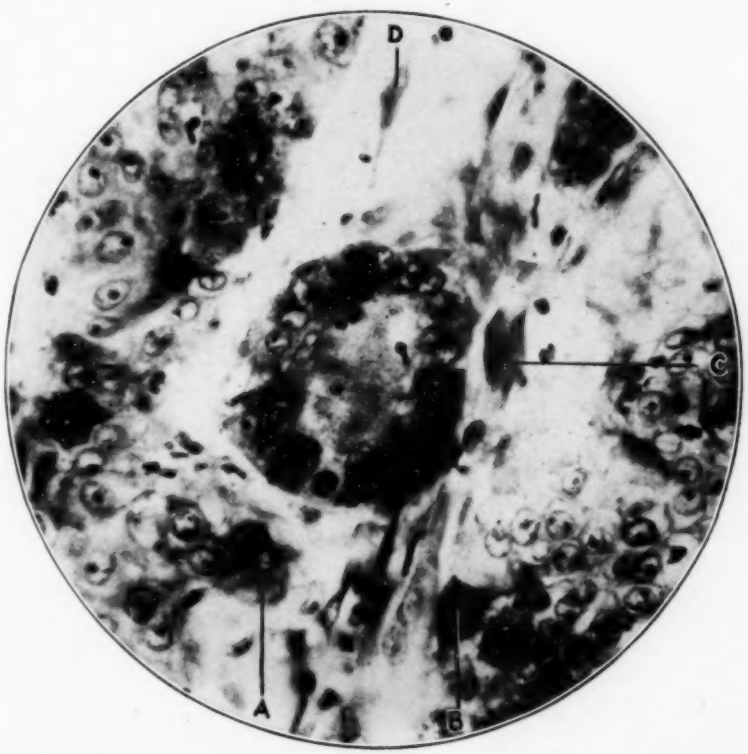

Fig. 3.—Types of altered ganglion cells in the invaded area. The periphery of the cell in the center contains a number of cancer cells; the central portion has numerous granules (Abbaustoffe) and several vacuoles containing lymphocytes and polymorphonuclear cells (use hand lens). At *A*, there is another ganglion of smaller size filled with cancer elements; at *B*, a dark homogeneous cell without inclusions; at *C*, a new formed capillary; at *D*, a fibroblast; the numerous round, pale bodies with distinct nucleoli are cancer cells. Thionin; × 480.

nuclear or mononuclear leukocytes and—of especial interest—cancer cells. In some instances these last occupied the entire ganglion cell body, including the processes (Fig. 2); in others they were collected

in a dense cluster in the center or in a crescentic mass at the periphery of the cell (Fig. 3).

With scarlet red, Marchi and lichtgrün-fuchsin stains minute fat-granules were demonstrable in the ganglion cells but were absent from the cancer cell bodies. With lichtgrün-fuchsin many ganglion cells showed numerous granules or droplets of fairly large size which stained various colors and may correspond to the so-called fuchsinophil (Fig. 4), lichtgrün and lipoid granules (Fig. 5).

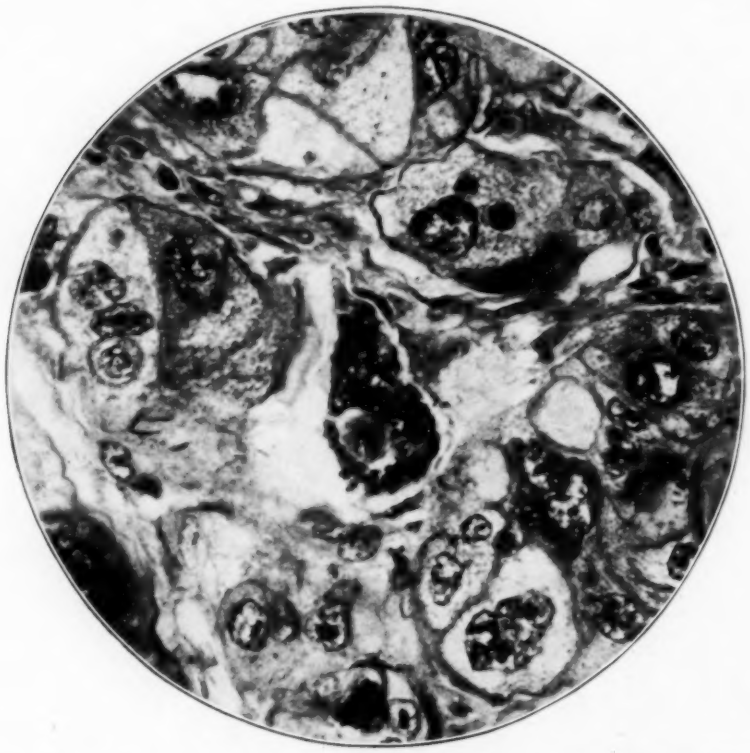

Fig. 4. — Ganglion cell in the center packed with granules (fuchsinophil, lichtgrün and other catabolic products). The rest are swollen and greatly liquefied ganglions. Lichtgrün-fuchsin; Alzheimer method VI; × 560.

The included cancer cells stained much more brilliantly than did the ganglion cells, and thus gave the section a deeply colored appearance. In places the greatly swollen ganglion cells were pressed so closely together as to form giant cells containing several nuclei. It was not always easy to differentiate between the nuclei of the host and those of the included cancer cells.

Some of the most damaged ganglion cells appeared structureless, colorless, devoid of chromatin and often without inclusions (Fig. 4)

but with a large pale nucleus, free from chromatin but possessing a membrane and visible nucleolus. Many could be recognized only by a careful study of the numerous transition types. So manifold were these that description is impossible. Some conception of the shape, size and general appearance may be gained from Figs. 3, 4 and 5. The process in general appeared to be progressive liquefaction and tumefaction with neuronophagy, the invaders being cancer cells, lymphocytes and polymorphonuclear leukocytes, the first being by far the most numerous.

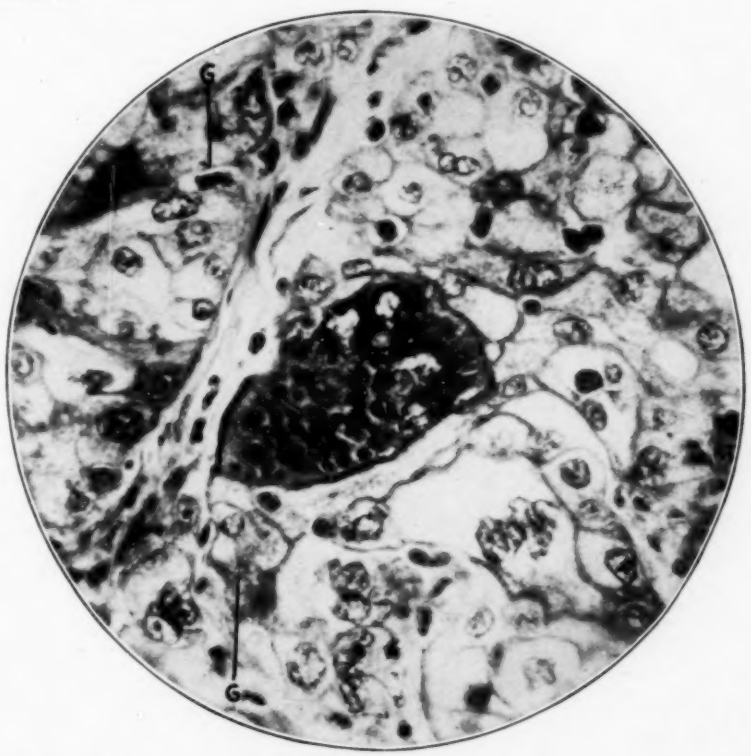

Fig. 5.—In the center of the photomicrograph is a large swollen ganglion cell invested with a connective tissue membrane. It contains large globules of lipoids and four vacuoles in which cancer cells can be seen with a hand lens; at *G G* are liquefied ganglion cells; the apical dendron of the upper one appears intensely dark and contains the nucleus. The rest of the picture shows numerous cancer nuclei within greatly changed and liquefied ganglion cells; some of these appear entirely colorless and empty. Lichtgrün-fuchsin; × 480.

It is noteworthy that within the tumor mass there was no glial proliferation. Instead, connective tissue fibers enclosed groups of nerve cells or even single cells. In the latter case the ganglion cell appeared to be invested with a connective tissue membrane (Fig. 5). The connective tissue was derived from the blood vessels and pial pro-

longations and often formed broad strands which usually were entirely devoid of carcinoma cells but contained many plasma cells, lymphocytes, polyblasts, polymorphonuclear leukocytes, fibroblasts and numerous gitter cells packed with lipoids (Fig. 2). Here and there a ganglion cell or glia cell was found. The former were shrunken, homogeneous and atrophic with obvious, tortuous processes and an oblong nucleus, poor in chromatin. The glia cells were less frequent and occurred with large cytoplasmic bodies or as glia nuclei lodged within ganglion cells.

Fig. 6.—Transition zone occupying the entire picture except a small sector of cancer tissue at *A*, above. It shows colloid masses, cytoplasmic glia (use hand lens), hyperemic vessels with hyperplastic adventitia and a colloid ring around a large blood vessel at the bottom. Bielschowsky stain counterstained with Alzheimer-Mann; × 40.

Zone of Demarcation.—In the zone of demarcation, between the area invaded by the carcinoma and the more normal appearing brain tissues, there were a few ganglion cells invaded by glia nuclei, and numerous other cells. Among these, plasma cells were especially prominent, some containing two typical and well stained nuclei; in others the nucleus showed only remnants of chromatin. Polyblasts, shrunken

polymorphonuclears and gitter cells were also numerous. In the majority of our cases a demarcation zone was absent and replaced by a transition zone (Fig. 6). Here the tissues were markedly rarefied, vacuolated and appeared as a so-called glia reticulum. Glia cells were prominent, with abundant cytoplasm, homogeneous and pale and an eccentric nucleus rich in chromatin. Blood vessels were numerous, the adventitial spaces distended and infiltrated with gitter cells, lymphocytes and even cancer cells. They were often surrounded by a ring of a colloid substance occupying the areas assigned to the spaces of His.

Fig. 7.—Microscopic cancer foci. Small blood vessels invested with carcinoma cells and surrounded by clear spaces. Alzheimer-Mann; × 70.

Such colloid material was not found in the tumor masses proper, the connective tissue stroma nor in the demarcation zone. It was common, however, and especially well developed in those cases in which no distinct demarcation zone was present. It appeared, then, in the form of islands of homogeneous, jelly-like material, much resembling ameboid glia (Fig. 6). In addition, there were present large numbers of amyloid bodies. Ganglion cells were present but were scanty in the transition zone. They were very pale and showed marked chromatolysis.

In some instances the transition zone was not pronounced but, with special stains (scarlet red, Alzheimer-Mann), it could be demonstrated as a narrow space filled with gitter cells, proliferated glia and, in some instances, cancer cells.

The transition zone may thus be regarded as an area in process of invasion by the tumor mass spreading by direct penetration, the tissues becoming so damaged as to offer little resistance. The demarcation zone, on the other hand, consisted of more vigorous elements which

Fig. 8.—An area outside the demarcation zone. The glia reticulum is marked; a blood vessel in the center shows a greatly rarefied brain tissue containing lymphocytes, plasma cells and gitter cells and is surrounded by a ring of syncytial glia. Bielschowsky stain counterstained with Alzheimer-Mann; × 170.

afforded some protection but yet, as will be seen, failed to save the rest of the brain from damage.

Separated, at times even remotely, from the main tumor mass were numerous microscopic foci of cancer cells (Fig. 7). Such foci consisted of a small blood vessel, infiltrated or occluded by large tumor cells, with nuclei very rich in chromatin and provided with a well developed membrane. Sometimes the cells were confined to the Virchow-

Robin spaces, but often they had broken through and, by proliferation, formed a larger focus. Then no trace of blood vessel could be detected, and the reactive and other phenomena approximated those of the main growth already described.

Regions Remote Even from Microscopic Foci.—These regions at first glance appeared normal. Closer study revealed universal pathologic changes. The ganglion cells were often swollen, with chromatolysis, eccentric nucleus, neuronophagia and fat infiltration. The glia cells were hypertrophied ("cytoplasmic") or proliferated in the

Fig. 9.—Necrotic areas with islands of carcinoma. The small area *A* shows a colorless center, devoid of vessels, surrounded by a zone containing a few degenerated cancer cells and an outer dense ring of well preserved cancer cells. Toluidin blue; × 36.

form of "rosettes." The vessels were dilated, and there were many new formed capillaries. Some vessels were surrounded by a ring of syncytial cytoplasmic glial cells (Fig. 8). Masses of pigment granules were contained within the proliferated adventitial and endothelial cells. The nerve fibers in places appeared swollen and spindle-shaped but not fragmented. In short, there was a generalized condition of toxic encephalitis.

Of the foregoing changes those most constant were: general toxic encephalitis, the colloid masses and the processes in the transition zone. In most of the cases the demarcation zone, as stated, was absent, and invasion of the ganglions by cancer cells was not observed. In these cases the tumor masses often presented large areas of central necrosis (Fig. 9) in which no cells could be detected. Surrounding such areas there were scattered, shrunken and poorly stained carcinoma cells (intermediate zone) and next to these again a larger zone of more or

Fig. 10.—Pia-arachnoid—distended, the subarachnoid space packed with cell bodies. *A,A,A,* foci of carcinoma separated from the proliferated pia (*C,C*) by an empty space which should be compared with the well formed pial covering of the brain at *B,D,D*—hyperplastic arachnoid. Van Gieson; × 60.

less well preserved cancer tissue, richly supplied with blood vessels. For the most part blood vessels were lacking in the central and intermediate zones; if present, they were dilated and enormously infiltrated with well formed cancer cells. Such infiltrated vessels stood out as beautifully stained islands in a colorless, necrotic mass (Fig. 9).

The Pia-Arachnoid and Choroid Plexus.—Whatever the type and extent of parenchymatous destruction, changes were constantly present

in the pia-arachnoid and the choroid plexus. The pial changes were most marked when the tumor almost reached the membrane. The pia-arachnoid then appeared as a mass of cancer tissue. Distant from the tumor, the membrane showed distended meshes with unusually prominent and numerous collagen fibers, the vessels were dilated and hyperemic, some new-formed with proliferating adventitial and endothelial cells and many fat globules. Often the meshes were scantily lined with cellular elements; in others these were present in large numbers (Fig. 10). Mesothelial cells predominated but fibroblasts,

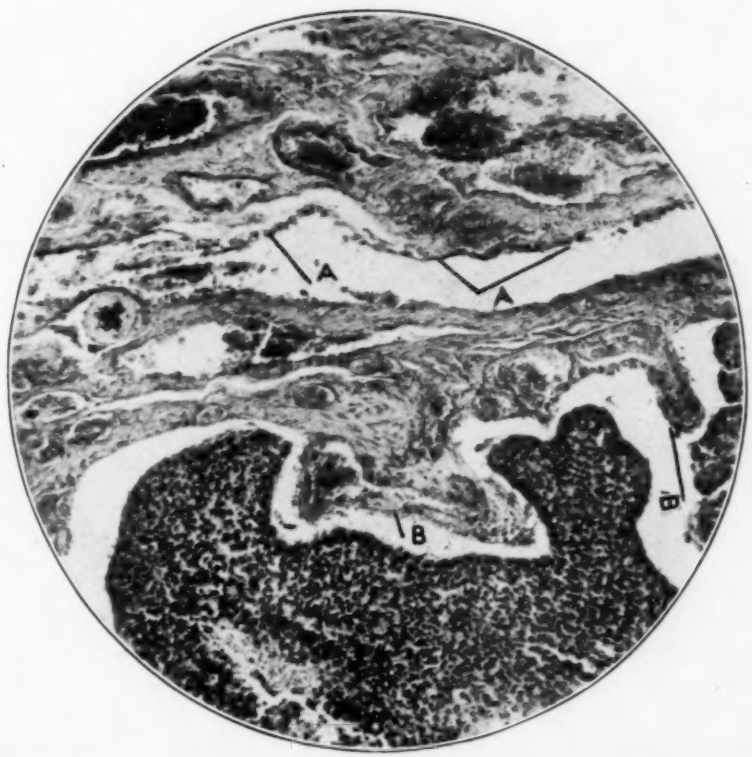

Fig. 11.—Choroid plexus invaded by carcinoma. *A,A,* epithelial tuft cells; *B,B,* tufts of the plexus, much resembling the villi of the arachnoid; the mass below is a carcinoma focus. Van Gieson; × 80.

lymphocytes, polyblasts and many gitter cells packed with lipoids were present. In addition, cells of distinctly epithelial character, much resembling carcinoma cells, were frequent. In advanced cases the arachnoid usually appeared hyperplastic (Fig. 10) and formed a dense connective tissue strand. The appearance in these membranes varied in different regions and cases but careful study always revealed pathologic changes.

In the choroid plexus the connective tissue stroma was usually proliferated and formed a homogeneous, hyperplastic strand, in some instances enormous. In one case it was invaded with foci of cancer cells (Fig. 11). In this case the tumor formed a protrusion of the brain substance into one lateral ventricle, compressing and almost invading the plexus. It is noteworthy that cancer cells were also found in the choroid plexus of the opposite lateral ventricle. In no other case were foci of cancer cells found; there were, however, somewhat indefinite mononuclear cells in the spaces between the blood vessels and the tuft cell covering.

The tuft cells sometimes formed several layers, were distinctly granular, large in size and brightly stained. The nuclei were rich in chromatin and located centrally or at the base of the cell. In the majority of the cells there existed a distinct vacuole of varying size which enclosed some amorphous substance. The blood vessels were hyperemic with hyperplastic walls, proliferated adventitial and hypertrophied endothelial cells. Colloid material, found so abundantly in the brain substance, was not observed here, and there was no thrombosis or hyaline degeneration. Calcareous bodies or psammomas were numerous in some cases.

SUMMARY AND DISCUSSION

1. In the invaded areas there were macroscopic and microscopic foci of carcinoma cells which in some cases invaded the ganglion cells. Glial or mesodermogenic reaction was absent.

2. There was a gradual propagation of the growth with formation of a transition, and more rarely a demarcation, zone with marked reaction phenomena.

3. Proliferation of connective tissue in the form of bands, derived from the pial intracerebral prolongations and blood vessels, outside the foci.

4. Toxic encephalitis throughout the brain.

5. Accumulation of catabolic substances (Abbaustoffe), especially colloid masses, around the vessels and in the tissues.

6. Changes in the vessels, pia and choroid plexus.

The changes enumerated in the foregoing—a combination of focal (tumor masses) and diffuse (encephalitic) lesions—were present in all our cases of cerebral carcinoma but were lacking in the meningeal neoplasms. In the latter, the brain substance proper was free from carcinoma cells. This is in accord with Pachantoni [9] who asserts that in the "majority" of cases of meningeal carcinoma (with the exception

9. Pachantoni, D.: Ueber diffuse Carcinomatose der weichen Hirnhäute, Arch. f. Psychiat. **49**:396, 1912.

of the case of Saxer) the brain was not involved. In one of our cases the most superficial strata were invaded. But in this case the meningeal infiltration was enormous, and the cells were probably spread by sheer pressure from the subarachnoid space into the adventitial spaces of the neighboring vessels. The deeper strata were entirely free from invading elements, and neither they nor remote areas of the brain showed signs of encephalitis or any other change. There is thus an essential difference between the cerebral and meningeal growths. This difference is most probably due to the direction of flow of the cerebrospinal fluid. The experimental work of Weed [10] and some facts of histopathology [11] demonstrate that the spinal fluid flows from the brain toward the subarachnoid space and possibly also toward the ventricles. This current carries with it the waste products of the brain, be these blood pigment from a hemorrhage, tubercles, fat substances or, as in the present instances, carcinoma cells and the products of their decomposition. These waste products are found in the subarachnoid space and there provoke reactive phenomena, mainly manifested by proliferation of mesothelial cells. The direction of flow of these tissue fluids will also explain the freedom of the brain tissue in carcinoma of the meninges. Unless the subarachnoid space is so packed with tumor cells that the pressure forces them into the adventitial spaces, there is complete immunity on the part of the brain, and where this condition does obtain only the most superficial layers are invaded.

Once within the brain tissues, the carcinoma cells give rise to reactive phenomena. These are evidenced mainly by connective tissue proliferation around or within the tumor mass. A demarcation zone may thus be formed and serve to limit the further extension of the growth. In the absence of such a zone, the surrounding tissues show changes indicative of gradual destruction before becoming invaded by and transformed into a mass of carcinoma cells. The further from the tumor, the less evidenced are these changes: rarefaction of the parenchyma with formation of a glia reticulum, hyperemia, deposits of colloid substances, lipoids and amyloid bodies. The further spread of the tumor may be limited by the development of a demarcation zone or

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10. Weed, L. H.: I. Studies on Cerebrospinal Fluid. II. The Theories of Drainage of Cerebrospinal Fluid with an Analysis of the Methods of Investigation, J. Med. Res. **26**:21, 1914-1915. III. The Pathways of Escape from the Subarachnoid Spaces with Particular Reference to the Arachnoid Villi, ibid., 51, 1914-1915. IV. The Dual Source of the Cerebrospinal Fluid, ibid., 93, 1914-1915. The Anatomical Consideration on Cerebrospinal Fluid, Anat. Rec. **12**:461, 1917-1918.

11. Hassin, G. B.: Histopathology of Carcinoma of the Cerebral Meninges, Arch. Neurol. & Psychiat. **1**:705 (June) 1919. Histopathology of Brain Abscess with Remarks on Intraspinal Therapy, ibid. **3**:616 (June) 1920.

be continued progressively by the formation of fresh transition zones. Even when a well marked demarcation zone is established, the carcinoma cells spreading along the perivascular spaces may lead to the formation of fresh miliary foci in regions more or less remote from the original focus and may even reach the pia-arachnoid. A cerebral carcinoma is thus propagated not only by direct continuity through the progressive infiltration of adjacent areas but also by way of metastases carried along the adventitial spaces of Virchow-Robin.

In addition to these two agencies—infiltration and metastasis—cerebral carcinoma also damages the brain tissues by chemical or toxic action. This is evidenced by the diffuse encephalitis. The toxic manifestations are especially marked in the foci themselves where the ganglion cells appear liquefied and invaded by cancer cells. Such cell invasion was not constant, being absent in the majority of our cases. It has not been mentioned in the literature. Fischer [6] alone described something resembling it in the envelopment of the bodies and processes of the ganglion cells by cancer cells. They filled up what he thinks are the pericellular spaces but did not invade the cells themselves.

In the majority of our cases no ganglion cells were found in the foci, which appeared necrotic or contained areas of so-called degenerative softening. Both the necrosis and softening are final stages in the parenchymal destruction. Their occurrence depends not only on the age of the focus but also on the virulence of the toxins elaborated by the tumor cells, deficient blood supply and purely mechanical factors (accumulation of vast numbers of cells). Of these factors—toxic, mechanical, trophic—the first is certainly the most important. In all probability it is responsible for many nervous and mental symptoms presented by patients with brain carcinoma which cannot be accounted for by focal lesions.

CONCLUSIONS

1. The brain lesions caused by carcinomatous growth are both focal and diffuse.

2. The focal lesions are due to direct invasion by carcinoma cells. The diffuse lesions are of the type of a toxic (noninfiltrative) encephalitis.

3. Reactive phenomena are mainly of connective tissue and may result in the formation of a demarcation zone.

4. In the absence of a demarcation zone a transition zone is constant and indicates destruction of the adjacent parenchyma prior to invasion by carcinoma cells.

5. Propagation of the tumor takes place by infiltration and along perivascular spaces.

6. Reactive phenomena occur in the pia-arachnoid and in the choroid plexus.

DISCUSSION

DR. ADOLF MEYER, Baltimore: These pictures of invasion of an area outside of the demarcation zone appear to me to be a demonstration of the chance for immigration into those regions, even if there is not the preformed space. In the examination of kindred specimens, I feel that the diffuse neighborhood invasions are relatively rare, when one deals with a large focal metastasis. It is evidently rather the unusual case that shows that biologic injection process.

With regard to the conception of an encephalitis, I am not quite as sympathetically disposed. I think it is extremely difficult to differentiate simple degenerative processes from anything which would be a toxic process of a more inflammatory character. It is difficult to know what circulatory or pressure disturbance may have been at the bottom of some of those neighborhood reactions. They are practically the same in all conditions which are space consuming, and that makes me rather suspicious of its being essentially a degenerative pressure effect and not so certainly a toxic effect.

DR. HASSIN, in closing: When I designated the changes in the cerebral tissues not invaded by the carcinoma toxic encephalitis, Dr. Singer strongly objected. He offered to call the condition degenerative encephalitis; but the latter term is as improper and misleading as that of degenerative myelitis, and therefore I retained the name "toxic."

The invasion of the so-called pericellular spaces by cancer cell bodies has been described by only one author, Oscar Fischer, of Prague. In 1904, he published a case of cerebral carcinoma in which the cancer cells were crowding the dilated spaces around the ganglion cells. Such spaces, however, are most likely artefacts.

METABOLISM STUDIES IN DEMENTIA PRAECOX AND MANIC-DEPRESSIVE INSANITY*

SECOND PAPER: GLYCEMIC REACTION TO THE INTRAMUSCULAR ADMINISTRATION OF EPINEPHRIN

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AND

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In view of the variant blood sugar tolerance reaction reported in dementia praecox and manic-depressive insanity [1] as compared to the so-called normal response, it was considered that it might prove of some value to study a group of such cases from the point of view of glycemic response to the intramuscular administration of epinephrin. Although the reaction in normal subjects to this reagent has not as yet been unequivocally established, fairly conclusive findings have been reported. Thus Hamman and Hirschman,[2] in a series of seven normal persons, who, after an overnight fast, were given 50 gm. (771.6 grains) of glucose by mouth, report the reaction as attaining its peak in one hour after the administration of from 0.66 to 1 mg. of epinephrin with complete subsidence at the end of the second hour, the reaction having been followed for three hours. Definitely delayed reaction was noted in persons with diabetes; and Cowie and Beaven [3] more recently, on the basis of data secured in the study of two normal subjects after the injection of 1 mg. of epinephrin, determined the reaction acme as occurring from the end of the first to the end of the second hour with subsidence by the end of the third hour. Estimates made at the end of the fifth hour showed a slight depression in the curve below the fasting level. In a series of influenza and influenzal pneumonia cases these authors found the reaction was definitely delayed, and on this basis they considered the possibility of endocrine dysfunction in such cases, particularly of the suprarenal system.

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* From the State Psychopathic Hospital, Ann Arbor, Mich.

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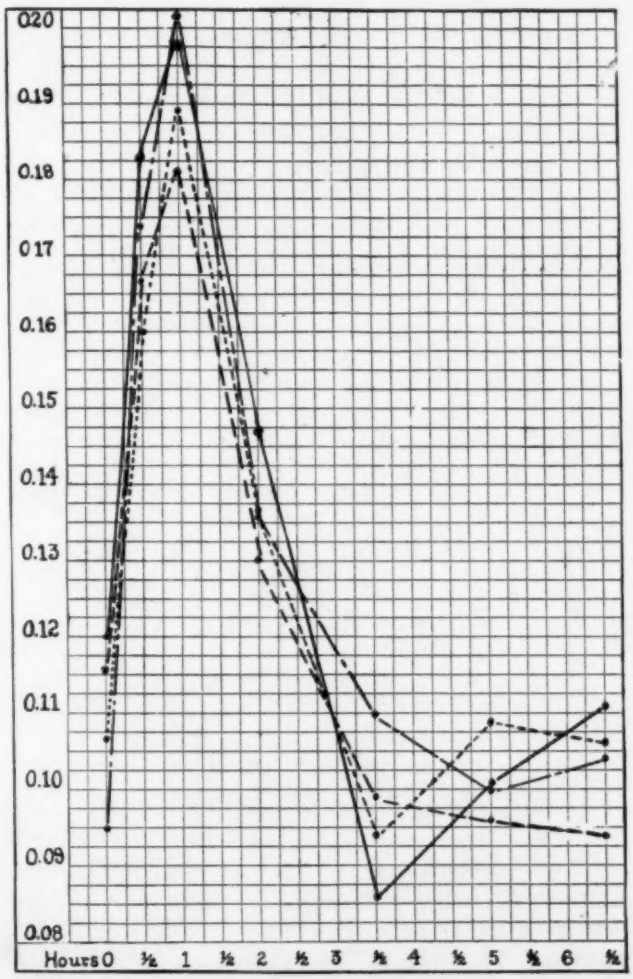
2. Hamman, L., and Hirschman, I.: Studies on Blood Sugar—Alimentary Hyperglycemia and Glycosuria as a Test of Sugar Tolerance, Arch. Int. Med. **20**:762 (Dec.) 1917.

3. Cowie, D. M., and Beaven, P. W.: On the Clinical Evidence of Involvement of the Suprarenal Glands in Influenza and Influenzal Pneumonia, Arch. Int. Med. **24**:78 (July) 1919.

PROCEDURE

Comprising the present series (Table 1) there were three normal controls, nine cases of dementia praecox (including simplex, hebephrenic, paranoid and catatonic types) and six cases of manic-depressive insanity (including three patients in the excited or agitated phase and



Composite graph of epinephrin glycemia. The continuous line indicates the blood sugar percentage in normal persons; the short and long dashes, in patients with dementia praecox; the short dashes, in manic-depressive (excited) patients; the long dashes, in manic-depressive (depressed) patients.

three in the depressed phase). The psychotic subjects were all in the acute phase of their specific disorders.

The exact procedure employed in this study may be detailed as follows: After an overnight fast (6 p. m. to 7 a. m.), initial or

control blood samples were drawn and 1 mg. of epinephrin (1 c.c. of epinephrin chlorid, Parke, Davis & Company) was administered intramuscularly. Following this, blood samples were drawn after half an hour, one hour, two hours, three and one-half hours, five hours, and six and one-half hours, and blood sugar determinations made essentially according to the Lewis-Benedict method, as described in full in an earlier paper by Raphael and Parsons.[1] No food was given during the experiment period, and the subjects were kept at absolute rest as far as possible.

Abstracts of Cases 6, 7, 9, 10 and 15 follow; abstracts of the remaining cases were prepared in connection with the first report, already mentioned, and may there be found.

TABLE 1.—SERIES OF NORMAL PERSONS AND PATIENTS STUDIED BY AUTHORS

Number	Case	Age	Sex	Type	Grade
Normal Subjects—					
1	W. A.	25	Male		
2	T. D.	38	Male		
3	A. N.	18	Male		
Psychotic Subjects—					
Dementia Praecox:					
4 (10) S.P.H. 2560	C. M.	22	Male	Simplex	Acute
5 (9) S.P.H. 2589	L. H.	19	Male	Hebephrenic	Acute
6 S.P.H. 3102	J. M.	21	Male	Hebephrenic	Acute
7 S.P.H. 3159	H. B.	29	Female	Hebephrenic	Acute
8 (11) S.P.H. 2528	H. T.	27	Female	Hebephrenic	Acute
9 S.P.H. 2987	B. K.	28	Female	Hebephrenic	Acute
10 S.P.H. 3144	M. T.	34	Female	Catatonic	Acute
11 (15) S.P.H. 2410	F. W.	20	Female	Paranoid	Acute
12 (8) S.P.H. 2560	N. S.	25	Male	Paranoid	Acute
Manic-Depressive Insanity:					
13 (22) S.P.H. 2610	R. W.	23	Male	Hypomanic	Acute
14 (29) S.P.H. 2597	A. R.	32	Female	Agitated depression	Acute
15 S.P.H. 3109	E. O.	29	Female	Manic	Acute
16 (25) S.P.H. 2566	R. R.	37	Female	Depressive	Acute
17 (23) S.P.H. 2582	M. L.	28	Female	Depressive	Acute
18 (24) S.P.H. 2583	M. P.	36	Female	Depressive	Acute

REPORT OF CASES

CASE 6.—Diagnosis: dementia praecox, hebephrenic type.

J. M., a young man, single, aged 21, was admitted to the hospital May 21, 1921. His mother and sister had been committed to the Newberry State Hospital, with cases diagnosed as dementia praecox. His personal history was negative until the beginning of the present trouble. For about three weeks prior to admission the patient had become seclusive, irritable, suspicious, destructive and impulsive, with ideas of reference and various somatic complaints. Under observation in the State Psychopathic Hospital the patient was found to be definitely autistic, poorly accessible, apparently disoriented and indifferent and had marked affective deterioration. There was also evidence of auditory hallucinosis of an essentially erotic nature, grimacing and silly, apparently unmotivated laughter, and an occasional homicidal impulse.

Physical and neurologic examinations were essentially negative.

At the time this study was made the psychiatric status was still definitely as described.

CASE 7.—Diagnosis: dementia praecox, hebephrenic type.

H. B., a man, single, aged 29, admitted to the hospital July 28, 1921, had a negative family history. His personal history was apparently negative until the beginning of the present trouble which was reported to have had its onset after an "indefinite illness" while he was in the service in 1918. He became disoriented, confused and hallucinated. Following admission to the State Psychopathic Hospital the patient was definitely autistic, disoriented, somewhat confused, obviously indifferent and apathetic and presented marked delusional thought content of an extremely fantastic nature associated with auditory and visual hallucinosis and a tendency toward attitudinizing of a symbolic nature, unmotivated laughter and lack of insight.

Physical and neurologic examinations were essentially negative. At the time this study was made the psychiatric status was still definitely as described.

CASE 9.—Diagnosis: dementia praecox, hebephrenic type.

B. K., a woman, single, aged 28, admitted to the hospital Dec. 19, 1920, had a negative family history with the exception of epileptiform attacks in a brother and "nervous trouble" in one sister. The patient was considered normal mentally. She had graduated from a normal school. Since then, until the beginning of the present trouble, she taught school or was engaged in responsible work of a clerical nature. From an early age the patient had been reported as shy, particularly with reference to the opposite sex, somewhat seclusive and reticent about personal matters and subject to frequent episodes of depression. In June, 1920, she suffered a short period of depression for several days, after which she became noisy, excited and definitely hallucinated, with a prominent delusional trend. After about six weeks the patient was found to have become somewhat apathetic. After admission to the State Psychopathic Hospital Dec. 11, 1920, she was poorly accessible, indifferent and apathetic with reference to her surroundings. She refused food and was untidy in her personal appearance. She exhibited a definitely schizophrenic trend with marked delusions somewhat fantastic in type, hallucinations, ideas of reference and influence, unmotivated laughter and evidence of mannerisms.

Physical, neurologic and laboratory examinations were negative.

At the time this study was made the patient had become somewhat less agitated but otherwise there was no change in the initial condition.

CASE 10.—Diagnosis: dementia praecox, catatonic type.

M. T., a woman, married, aged 34, admitted to the hospital July 13, 1921, had a negative family history. Her infancy and childhood were reported as essentially normal. She was fairly successful in school, having attained the sixth grade at the age of 12. She married at the age of 27 and had one child. She had complained of vague gastro-intestinal disturbance for some years and had never been really sturdy. About a year ago the patient had become somewhat exhausted physically, indifferent and apathetic, showing definite evidence of delusional trend and hallucinosis associated with episodes of acute excitement with vague paranoid trend and evidence of suicidal intent. Following admission to the State Psychopathic Hospital on July 13, 1921, the patient was extremely negativistic, resistive, mute and untidy. She refused food and frequently drooled. The patient was definitely autistic and assumed stereotyped postures.

Physical, neurologic and laboratory examinations were negative.

At the time this study was made the psychiatric status was definitely as described.

CASE 15.—Diagnosis: Manic-depressive insanity; manic insanity, third attack.

E. O., a woman, married, aged 29, was admitted to the hospital May 31, 1921. Her maternal grandfather was reported to have had a "nervous breakdown" at 50, lasting six months. Her paternal grandmother was reported to have suffered a psychotic episode characterized by delusional trend, following confinement. The maternal line in general is reported as prone to "emotional weakness." Her personal history was negative with the exception of typhoid at the age of 16. She was married at 21 and had four children. She is reported to have been sociable, of pleasant disposition and to have had many personal friends. She suffered a mild attack of depression while at school at the age of 20, lasting two weeks. The second attack of depression was noted in 1920, following influenza complicated by sinusitis, during which she was committed to this hospital, having been discharged as improved on April 13, 1920. The present attack began about December, 1920, and was characterized by restlessness, instability of purpose and social overactivity. The patient was admitted to the State Psychopathic Hospital May 13, 1921, in a state typically characteristic of manic excitement, showing marked flight of ideas, very much increased psychomotor activity, extremely hypersthenic trend, distractibility and irritability on interference. She did not eat unless fed, was untidy about her personal appearance and slept little.

Physical, neurologic and laboratory examinations were negative.

At the time this study was made the psychiatric status was definitely as described.

DISCUSSION

The data secured in this study were tabulated as indicated in Table 2. It will be noted that there is sufficient agreement as respects the individual group cases to warrant the use of a composite graph for the purpose of securing more direct comparison.

On analysis it appears that in two of the normal subjects the reaction acme was reached at the end of thirty minutes, and in one at the end of one hour; in the case of the psychotic subjects, with one exception (Case 8), the reaction peak seems to have occurred at the end of one hour. Among the normal persons subsidence occurred in one case at the end of the second hour, but in the other two did not take place until after three and one-half hours, thus affording essential agreement with the observations of both Hamman and Hirschman and Cowie and Beaven. It should be noted, too, that in these normal cases the point of minimum glycemia or what might be termed the reaction pit is definitely below the individual fasting level and was noted in all three cases at the end of the three and one-half hour period, and that following this there is seen to be a somewhat gradual but definite return to the initial level which seems to have been practically reattained by the end of six and one-half hours. This drop below the fasting level or reaction pit with subsequent rebound, although partially indicated in the work of Hamman and Hirschman and of Cowie and Beaven, had not been specifically described by these authors.

As regards the response among the psychotic subjects, it will be noted that, although the general topography of the reaction curve

definitely resembles that noted in the controls, particularly through the first three and one-half hours, there are nevertheless certain definite points of difference. Thus it seems that in the excited and depressed phases of the manic-depressive group the point of maximum glycemia is below the acme level reached by the normal cases and the cases of dementia praecox. Also, and of somewhat more importance, it will be noted that the excited patients in the manic-depressive group seem to manifest clearly the control trend, presenting the characteristic subfasting level reaction pit described in this group followed by definite rebound to just above the initial level. In patients with

TABLE 2.—CHRONOLOGIC ANALYSIS OF EPINEPHRIN GLYCEMIA (PERCENTAGE)

Case	Fasting	After ½ Hr.	After 1 Hr.	After 2 Hrs.	After 3½ Hrs	After 5 Hrs.	After 6½ Hrs.
Normal Subjects—							
1. W. A.	0.115	0.120	0.200	0.180	0.076	0.080	0.100
2. T. D.	0.120	0.205	0.192	0.156	0.095	0.105	0.115
3. A. N.	0.125	0.225	0.200	0.105	0.089	0.120	0.120
Average	0.120	0.183	0.198	0.147	0.086	0.101	0.111
Psychotic Subjects—							
Dementia Praecox:							
4. C. M.	0.095	0.105	0.120	0.110	0.100	0.080	0.100
5. L. H.	0.084	0.130	0.185	0.112	0.198	0.110	0.100
6. J. M.	0.116	0.172	0.215	0.165	0.096	0.114	0.117
7. H. B.	0.122	0.186	0.196	0.113	0.090	0.129	0.135
8. H. T.	0.074	0.180	0.166	0.070	0.172	0.082	0.071
9. B. K.	0.122	0.238	0.266	0.173	0.108	0.102	0.118
10. M. T.	0.094	0.239	0.279	0.266	0.135	.....	0.095
11. F. W.	0.085	0.182	0.222	0.112	0.072	0 076	0 098
12. N. S.	0.080	0.140	0.166	0.128	0.120	0.110	0.110
Average	0.095	0.174	0.201	0.137	0.110	0.100	0.104
Manic-Depressive Insanity:							
Excited type:							
13. R. W.	0.100	0.145	0.190	0.105	0.051	0.098	0.095
14. A. R.	0.094	0.125	0.125	0.120	0.115	0.120	0.090
15. E. O.	0.129	0.212	0.253	0.188	0.111	0.109	0.134
Average	0.107	0.160	0.189	0.136	0.092	0.109	0.106
Depressive type:							
16. R. R.	0.110	0.181	0.195	0.140	0.085	0.088	0.100
17. M. L.	0.120	0.180	0.200	0.125	0.092	0.092	0.084
18. M. P.	0.120	0.140	0.150	0.125	0.120	0.110	0.100
Average	0.116	0.167	0.181	0.130	0.099	0.096	0.094

dementia praecox and in the depressed phase of the manic-depressive psychosis, the drop at the three and one-half hour point is definitely less than that of the controls and of the excited manic patients, and instead of showing a rebound trend from this point, continues to drop gradually. In the depressed phase of manic-depressive psychosis there is no tendency to rebound, and in the dementia praecox cases practically none. In these groups the reaction pit is practically absent, and among the praecoxes the curve does not descend below the original fasting level. These departures may possibly be of significance from the point of view of specific metabolic difference, particularly so in view of the apparent deviation as already reported in such cases, in blood sugar

Irrigation with solutions containing sodium and calcium had the same effect as irrigation with the modified Ringer's solution. Solutions of sodium and potassium were highly toxic and caused death before the completion of one hour's irrigation. The toxic effects were practically the same as those of pure sodium chlorid solutions.

It occurred to us that since an absence of calcium in the irrigating fluid was accompanied by such great irritability and even maniacal attacks in cats, that the maniacal activity of patients with manic-depressive insanity, though the symptoms are hardly comparable, might be associated with a deficiency of calcium in the blood or spinal fluid or both. An excess of calcium might be associated with the depressed phase of the same type of patient, and if such an association should exist, it would be demonstrable. Furthermore, if the association exists, restoration of the salt balance by the use of calcium in manic states and of sodium in the depressed states might be of therapeutic value. Several simple methods, recently reported, have made it possible to determine with a fair degree of accuracy the amounts of sodium, potassium, calcium and magnesium in small quantities of blood or spinal fluid.

The results of the usual routine examination of the blood and spinal fluid furnished the material, only frank cases being used. Both fluids were collected at the same time, in the morning before breakfast, and were examined at once. The technic employed was that of Kramer and Tisdall.[2] The blood was defibrinated as soon as drawn and centrifugalized. The clear serum was pipetted off and the analyses begun immediately. Eight cubic centimeters of serum and 12 c.c. of spinal fluid were required and were distributed as follows:

For Sodium

2 c.c. serum	2 c.c. fluid
1 c.c. plus 1 c.c. sodium solution	1 c.c. fluid plus 1 c.c. sodium solution
2 c.c. sodium solution	

For Potassium

1 c.c. serum	2 c.c. fluid
1 c.c. serum plus 1 c.c. potassium solution	1 c.c. fluid plus 1 c.c. potassium solution
2 c.c. potassium solution	

For Calcium and Magnesium

2 c.c. serum	4 c.c. fluid
1 c.c. serum plus 1 c.c. each of calcium and magnesium solutions	2 c.c. fluid plus 1 c.c. each of calcium and magnesium solutions
1 c.c. calcium plus 1 c.c. magnesium solution	

The control solutions contained sodium, 2.5 mg. per c.c.; potassium, 0.2 mg. per c.c.; calcium, 1 mg. per c.c.; magnesium, 0.025 mg. per c.c.

The errors in analyses as checked by the controls were in no case over 3 per cent. and the average was 1 + per cent.

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2. Kramer and Tisdall: Bull. Johns Hopkins Hosp. **32**:44, 1921; J. Biol. Chem. **46**:339, 472, 1921.

The potassium content of the spinal fluid as reported varies considerably. Mestrezat [3] found 20.8 mg. per 100 c.c.. of 20 mixed normal spinal fluids. Myers [4] found an average of 19.2 mg. per 100 c.c. in fifteen cases of various psychoses, eleven of which were cases of paresis. He calls attention to the necessity of obtaining the fluid before death. Rosenbloom and Andrews [5] tabulated the estimations found in the literature. The amounts varied from 14.1 to 118.9 mg. per 100 c.c. These authors found amounts ranging from 14.1 to 111.9 mg. in a series of cases including three normal subjects, three cases of paresis, eight of cerebrospinal syphilis, five of dementia præcox, one each of tertiary spyhilis, typhoid fever, presenile dementia, chronic alcoholism, encephalitis and meningitis and two each of tuberculous meningitis, acute alcoholism and neurasthenia.

The sodium content is given by Mestrezat as 323 mg. per 100 c.c. and the magnesium as 3.0 mg. The calcium content is generally accepted as being between 4.5 and 6.0 mg. per 100 c.c.[6] The potassium content of serum as reported is more constant in amount. Schmidt [7] gives 31 and 33 mg. for two normal subjects, Macallum,[8] 19 to 21 mg., Myers and Short [9] rather less than 20 mg. These authors point out the necessity of obtaining the serum almost immediately from the clot and of obtaining the blood during life. Kramer and Tisdall [2] found 18 to 21 mg.: Simon,[10] 32.1 to 33.3 mg. Macallum points out that Schmidt's figures are rather high. This is true also of Simon's figures.

The sodium found in serum by Kramer and Tisdall [2] averaged 337 mg. per 100 c.c. in ten normal subjects, nine of whom were under 11 years of age, and one was an adult. Simon [10] gives 319 mg.; Schmidt, 344 mg., and Mestrezat, 255 mg. per 100 c.c.

The magnesium in serum found by Kramer and Tisdall in four normal adult males varied from 2.1 to 2.9 mg. and averaged 2.7 mg. per 100 c.c. Mestrezat gives 4.4 mg. as normal; Marriott and Haessler [11] 2.2 to 3.5 mg. and Denis,[12] 1.6 to 3.5 mg.

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4. Myers: J. Biol. Chem. **6**:115, 1909.
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6. Halverson, Mohler and Bergeim: J. Biol. Chem. **30**:121, 1917; **29**:337, 1917; **32**:159, 1917. Denis and Minot: Ibid. **41**:359, 1920. Kramer and Howland: Ibid. **43**:35, 1920. Jones and Nye: Ibid. **47**:321, 1921. Marriott and Haessler: Ibid. **32**:233, 1917.
7. Schmidt, quoted by Myers and Short: J. Biol. Chem. **48**:83, 1921.
8. Macallum: Tr. College Phys., Philadelphia, Ser. 3, **39**:286, 1917.
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10. Simon: Text Book of Physiological Chemistry, Ed. 3, Lea Brothers, 1907, p. 334.
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2 c.c. sodium solution	

For Potassium

1 c.c. serum	2 c.c. fluid
1 c.c. serum plus 1 c.c. potassium solution	1 c.c. fluid plus 1 c.c. potassium solution
2 c.c. potassium solution	

For Calcium and Magnesium

2 c.c. serum	4 c.c. fluid
1 c.c. serum plus 1 c.c. each of calcium and magnesium solutions	2 c.c. fluid plus 1 c.c. each of calcium and magnesium solutions
1 c.c. calcium plus 1 c.c. magnesium solution	

The control solutions contained sodium, 2.5 mg. per c.c.; potassium, 0.2 mg. per c.c.; calcium, 1 mg. per c.c.; magnesium, 0.025 mg. per c.c.

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The sodium found in serum by Kramer and Tisdall [2] averaged 337 mg. per 100 c.c. in ten normal subjects, nine of whom were under 11 years of age, and one was an adult. Simon [10] gives 319 mg.; Schmidt, 344 mg., and Mestrezat, 255 mg. per 100 c.c.

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9. Myers and Short: J. Biol. Chem. **48**:83, 1921.
10. Simon: Text Book of Physiological Chemistry, Ed. 3, Lea Brothers, 1907, p. 334.
11. Marriott and Haessler: J. Biol. Chem. **32**:233, 1917.
12. Denis: J. Biol. Chem. **41**:363, 1920.

The calcium content varies from 9 to 12 mg. per 100 c.c.

The tables include only those cases diagnosed as manic-depressive psychoses, manic or depressed phase. The Wassermann reaction, globulin tests and colloidal gold curve were negative in all cases.

TABLE 1.—Sodium, Potassium, Calcium and Magnesium in Blood and Spinal Fluid of Patients Suffering from the Manic Phase of Manic-Depressive Insanity

Case	Age	Duration		Sodium		Potassium		Calcium		Magnesium	
		Total	Attack	Blood, Mg.	Fluid, Mg.	Blood, Mg.	Fluid, Mg.	Blood, Mg.	Fluid, Mg.	Blood, Mg.	Fluid, Mg.
11361	18	4 yr.	6 mo.	322	325	21.2	12.9	11.2	5.0	2.3	2.4
11385	20	3 mo.	3 mo.	334	340	18.6	11.6	11.0	5.0	2.7	2.7
11301	22	6 mo.	6 mo.	330	330	20.6	13.0	10.5	5.1	2.3	2.3
11327	23	6 mo.	6 mo.	330	330	30.5	15.0	10.1	5.0	2.4	2.3
11249	24	3 mo.	3 mo.	334	331	19.5	14.0	9.8	5.0	2.4	2.1
11407	26	8 yr.	3 mo.	331	335	18.6	11.6	11.0	5.0	2.3	2.4
11808	26	6 yr.	6 mo.	333	331	20.5	12.6	10.0	5.0	2.1	2.4
11120	26	5 mo.	5 mo.	334	340	23.2	13.0	10.0	5.0	2.2	2.3
11340	26	5 mo.	5 mo.	329	330	20.0	14.0	10.0	5.0	2.4	2.3
11273	33	2 yr.	6 mo.	328	322	21.6	12.9	9.9	5.1	2.4	2.2
11083	35	1 yr.	1 mo.	322	324	20.6	13.2	10.0	5.1	2.3	2.3
11373	40	6 yr.	7 mo.	343	346	25.0	11.0	11.5	5.5	2.1	2.3
11344	52	4 yr.	2 mo.	337	337	23.0	12.0	12.0	5.5	2.3	2.3
8475	54	19 yr.	2 wk.	343	343	24.0	13.1	11.0	6.0	2.4	2.4
11322	54	18 yr.	2 mo.	325	327	23.0	13.5	10.0	5.2	2.4	2.4
11292	57	4 yr.	4 mo.	339	343	19.5	12.1	9.5	5.0	2.6	2.5
7322	60	12 yr.	1 mo.	329	329	19.0	12.4	10.0	5.0	2.3	2.3
Average				332	333	21.7	12.8	10.4	5.2	2.4	2.4
Maximum				343	346	30.5	14.0	12.0	6.0	2.7	2.7
Minimum				322	322	18.6	11.0	9.5	5.0	2.1	2.1

TABLE 2.—Sodium, Potassium, Calcium and Magnesium in Blood and Spinal Fluid of Patients Suffering from the Depressed Phase of Manic-Depressive Insanity

Case	Age	Duration		Sodium		Potassium		Calcium		Magnesium	
		Total	Attack	Blood, Mg.	Fluid, Mg.	Blood, Mg.	Fluid, Mg.	Blood, Mg.	Fluid, Mg.	Blood, Mg.	Fluid, Mg.
11358	18	4 mo.	4 mo.	297	303	20.0	12.1	9.0	5.0	2.7	2.7
11377	25	3 mo.	3 mo.	343	346	19.5	12.1	10.0	5.5	2.5	2.6
11422	30	5 mo.	5 mo.	334	328	19.2	12.1	9.0	5.1	2.4	2.7
11283	32	7 mo.	7 mo.	328	329	22.0	13.0	12.7	6.0	2.3	2.4
11083	35	1 yr.	2 wk.	339	341	21.5	13.0	12.0	6.0	2.3	2.3
11274	38	7 mo.	7 mo.	334	354	32.0	15.0	11.7	5.8	2.4	2.4
11081	38	1 yr.	1 yr.	328	314	23.1	11.6	10.0	5.0	2.7	2.7
11315	40	6 mo.	6 mo.	334	334	19.2	13.3	10.0	6.0	2.3	2.3
9200	41	10 yr.	2 yr.	334	340	20.7	12.1	10.1	5.0	2.4	2.4
11190	57	3 mo.	3 mo.	329	315	22.7	12.9	11.3	5.0	2.4	2.5
Average				330	328	22.0	12.7	10.6	5.4	2.4	2.5
Maximum				343	346	32.0	15.0	12.7	6.0	2.7	2.7
Minimum				297	303	19.2	11.6	9.0	5.0	2.3	2.3
Average, manics				330	328	22.0	12.7	10.6	5.4	2.4	2.5
Average, depressed				332	333	21.7	12.8	10.4	5.2	2.4	2.4

Seventeen cases of mania and ten of depression are recorded. The duration of the present attack varies from two weeks to seven months in patients suffering from the manic phase of manic-depressive psychosis and from two weeks to two years in those suffering from the depressed phase. The ages varied from 18 to 60 years.

It is quite evident that there is no variation of the calcium content from the normal in either mania or depression. There is distinctly less potassium in the fluid than has been reported by others in conditions other than manic-depressive insanity. A number of determinations, not included in the tables, were made with the fluid from patients with paresis, dementia præcox, epilepsy and primary lateral sclerosis. The findings were the same as those given in the tables. A sufficient number of observations on the sodium, potassium and magnesium content of normal spinal fluid have not been recorded to warrant any conclusions regarding the significance of the potassium findings in our cases.

SUMMARY

In order to determine whether the manic and depressed phases of manic-depressive insanity are associated with an alteration of the normal balance of sodium, potassium, calcium and magnesium in the blood and spinal fluid, analyses were made of these two fluids in seventeen cases of mania and in ten of depression. The average of these elements was practically the same in both states, and the individual variations from the average were small. The average sodium content of the blood and fluid in mania was 332 and 333 mg. and in depression, 330 and 328 mg. The results with potassium were also constant—mania, blood and fluid, 21.7 and 12.8 mg.; depression, 22 and 12.7 mg. The blood and fluid calcium in mania was 10.4 and 5.2 mg. and in depression, 10.6 and 5.4 mg. Magnesium in mania showed 2.4 mg. for the blood and the same amount for the fluid; in depression the figures were 2.4 and 2.5 mg. The normal calcium content of the blood and spinal fluid may be considered as having been established, but reports of the sodium, potassium and magnesium content of the blood and more especially of the spinal fluid are unfortunately few, and the results are conflicting. In the absence of any long series of analyses of normal blood and spinal fluid for the foregoing three elements, no conclusions regarding our findings can be drawn. With respect to calcium our results show that in the cases here recorded there was no variation from the normal in either blood or spinal fluid.

SUGAR TOLERANCE IN DEMENTIA PRAECOX AND OTHER MENTAL DISORDERS

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MADISON, WIS.

Normally during a fasting period the blood sugar maintains a fairly constant level. The figures for normal persons obtained by various investigators are: Bang,[1] 0.10 per cent.; Myers and Bailey[2] (500 cases), 0.09 to 0.11 per cent.; Williams and Humphrey[3] (thirty-nine cases), 0.11 per cent. and (seventy-four cases) 0.107 per cent.; Liefman and Stern,[4] 0.105 per cent. Weston,[5] in a series of mental cases, found a blood sugar content ranging from 0.085 to 0.122 per cent., figures well within normal limits.

The blood sugar content may vary from a variety of causes. Not only does diet affect the sugar concentration but, according to Lusk[6] and Strouse,[7] variations were seemingly associated with the season of the year. Emotional states are likewise associated with changes in blood sugar concentration. Such effects were demonstrated in some of our cases. This is in accord with the observation of glycosuria during excitement by Cannon[8] and by Bohm and Hoffman[9] following painful stimulation of animals.

We, therefore, decided to note the emotional state, to insist on a preparatory period of fasting for at least twelve hours, and to have the patient maintain a recumbent position in bed under conditions of comfortable room temperature.

A normal reaction following the feeding of 100 gm. of glucose is as follows: During the first one-half hour the blood sugar rises and attains its highest level between one-half and one hour after the feeding. This rise is rarely more than from 0.04 to 0.05 per cent. Following the rise

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1. Bang, I.: Der Blutzucker, Wiesbaden, 1913.
2. Myers and Bailey: J. Biol. Chem. **24**:152, 1916.
3. Williams, J. R., and Humphrey, E. M.: Arch. Int. Med. **23**:537, 1919.
4. Liefman and Stern: Biol. Chem. Ztschr. **1**:301, 1906.
5. Weston, Paul G.: Analyses of Blood of Insane Patients, Arch. Neurol. & Psychiat. **3**:147 (Feb.) 1920.
6. Lusk, G.: Elements of the Science of Nutrition, Ed. 2, Philadelphia, W. B. Saunders Company, 1910.
7. Strouse, S.: Observations on Alimentary Hyperglycemia, Arch. Int. Med. **26**:759 (Dec.) 1920.
8. Cannon, W. B.: Bodily Changes in Pain, Fear, Hunger and Rage, New York, D. Appleton & Co., 1920.
9. Bohm and Hoffman in Cannon: Bodily Changes in Pain, Fear, Hunger and Rage, New York, D. Appleton & Co., 1920.

during the first hour there is a gradual fall until the concentration reaches its initial level, usually in from two and one-half to three hours after the feeding.

The earlier investigations of sugar tolerance were made in diseases in which disturbance of carbohydrate metabolism is the chief manifestation. Patients with diabetes gave a decidedly abnormal response after a glucose meal. The blood sugar rose slowly but reached a high concentration between the first and second hour after feeding. The rise was far above the normal and the high concentration was maintained over a much longer period. The initial level was rarely approached at the end of the third hour. In some cases a high concentration was maintained from four to five hours.

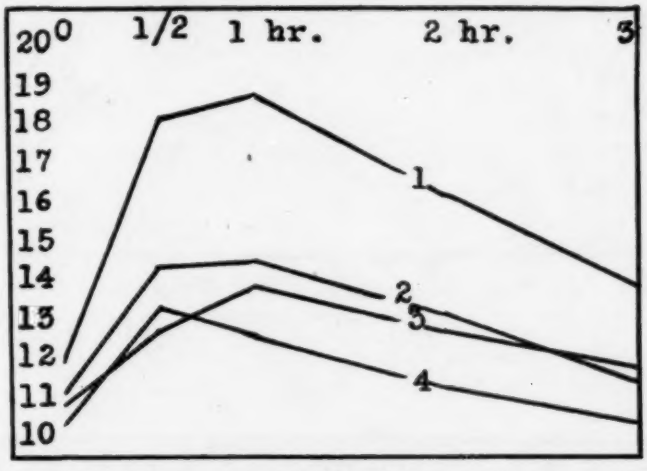

Chart 1.—The average curves of (1) catatonic patients, (2) hebephrenic patients, (3) patients with simple deteriorating praecox, and (4) patients with paresis.

Diabetes shows the highest blood sugar concentration in any disease so far reported and may reach 0.3 per cent.

A person with hyperthyroidism has also been shown to respond differently than a normal person, by Hamman and Hirschman,[10] Janney and Isaacson,[11] Geyelin,[12] Cummings and Pines,[13] Pemperton and Foster,[14] and others. In this condition the blood sugar following a sugar meal rises rapidly and reaches its highest concentration usually within the first hour; this high point averages above 0.2 per cent. During the succeeding two and one-half hours the blood sugar gradually

10. Hamman, L., and Hirschman, I. I.: Arch. Int. Med. **20**:176, 1917.
11. Janney, N. W., and Isaacson, V. I.: Arch. Int. Med. **22**:160, 1918.
12. Geyelin, H. R.: Arch. Int. Med. **16**:975, 1915.
13. Cummings, R. I., and Pines, G.: Arch. Int. Med. **19**:777, 1917.
14. Pemperton, R., and Foster, G. L.: Arch. Int. Med. **25**:243, 1920.

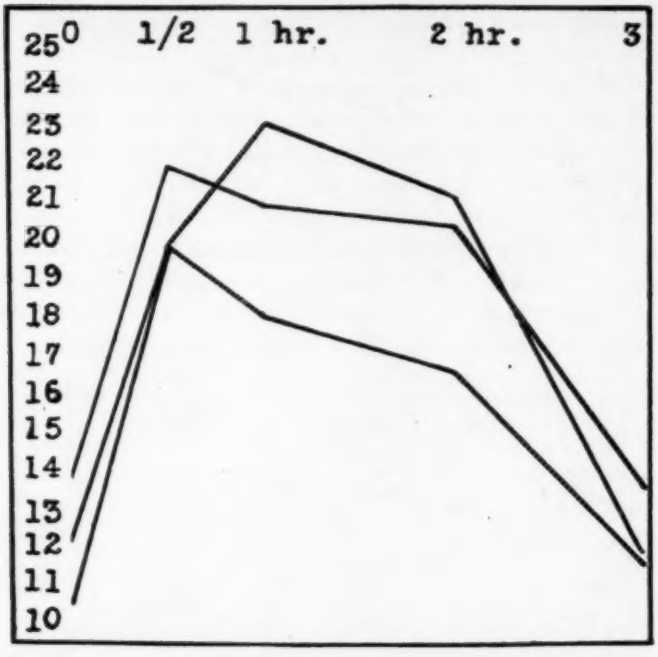

Chart 2 (Case C4).—This chart shows the similarity of response in one case of catatonia—three examinations at intervals of over four weeks.

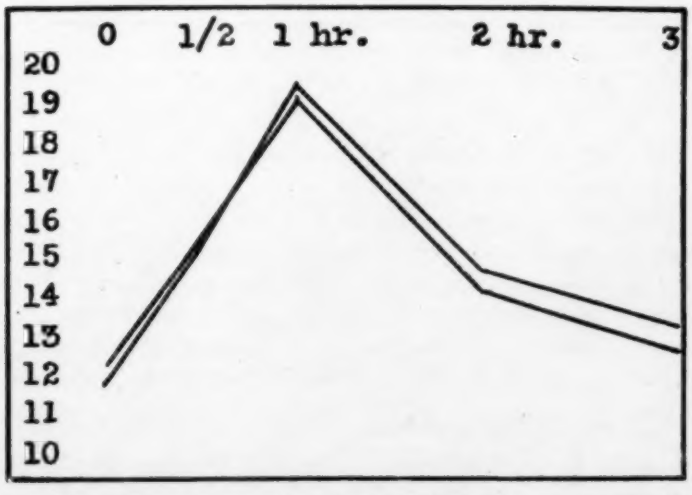

Chart 3 (Case C9, Catatonia).—Close parallelism in results of two examinations made at intervals of two weeks.

falls and approaches the initial level at the end of the third hour. These two types of response to sugar feeding are found in conditions of relatively low sugar tolerance; both show glycosuria after carbohydrate feeding. Patients with diseases of the pituitary gland and hypothyroid states show high sugar tolerance. The characteristic of this group is a reaction curve of less than normal as reported by Brock and Kaw,[15] Janney, Goodhart and Isaacson,[16] McCrudden and Sargent,[17] Knopfelmacher,[18] and others.

It may therefore be regarded as well established that certain endocrine disturbances are rather constantly associated with disturbance of carbohydrate metabolism; furthermore, that disturbance of carbohydrate metabolism can be demonstrated by tests of sugar tolerance, using as a method of investigation the hyperglycemia which follows a glucose meal.

The association of endocrine activity with mental development and mental states after maturity, the prominent rôle claimed for the endocrine glands in carbohydrate metabolism and the variations from normal reactions in clear endocrine dysfunctions, already quoted, suggested the use of this test to investigate internal gland disturbance in certain mental diseases.

Kooy, quoting W. F. Menzies,[19] reported that patients with melancholia show an abnormal response in the blood sugar for a two hour period following breakfast. Other than this we have found only an occasional case of mental disease, one paretic and several epileptic cases included among the cases reported by other investigators.

TECHNIC OF TEST

The work here reported began in November, 1920. A large series of blood examinations was made in which the method of Myers-Bailey[20] was compared with Benedict's modification[21] of the Lewis-Benedict method. It was decided to use the latter in our investigation.

Glucose was administered in 50 per cent. solution flavored with lemon juice and chilled with ice. The dose was 1.75 gm. per kilo of body weight. The feeding was given in the morning after fasting for from twelve to fourteen hours. All subjects were kept in bed

15. Brock, S., and Kaw, W. E.: Arch. Int. Med. **27**:1, 1921.
16. Janney, N. W.: Goodhart, S. P., and Isaacson, V. I.: Arch. Int. Med. **21**:188, 1917.
17. McCrudden, F. H., and Sargent, C. S.: Arch. Int. Med. **17**:465, 1916.
18. Knopfelmacher, W.: Wien. klin. Wchnschr. **17**:244, 1904.
19. Menzies, W. F.: J. Ment. Sc. **64**:275, 1920.
20. Myers and Bailey: J. Biol. Chem. **24**:147, 1916.
21. Benedict: Benedict's Modification of the Lewis and Benedict Method, J. Biol.Chem. **34**:203, 1918.

throughout the period of the test. Urine examinations were made on specimens voided during the three hours of observation. Approximately 3 to 4 c.c. of blood were taken from a vein and oxalated at once in a test tube. One sample was taken a few minutes before feeding the glucose. Subsequent samples were taken one-half hour, one, two and three hours after the glucose meal. Bedside notes were made on the emotional state, muscular activity, etc. The blood samples were all examined shortly after they were obtained, and the results are given in grams per cent.

TABLE 1.—Glucose Test in Cases of Dementia Praecox: Hebephrenic Type

Case No.	Before Feeding	½ Hour Interval	1 Hour Interval	2 Hour Interval	3 Hour Interval	Total Rise	Period of Rise
D 1	0.094	0.125	0.145	0.122	0.12	0.051	1 hour
	0.102	0.136	0.158	0.140	0.11	0.056	1 hour
D 2	0.122	0.150	0.132	0.120	0.115	0.028	½ hour
D 3	0.110	0.146	0.115	0.115	0.102	0.036	½ hour
D 4	0.100	0.130	0.128	0.128	0.122	0.030	½ hour
D 5	0.100	0.126	0.138	0.130	0.121	0.038	1 hour
D 6	0.095	0.137	0.128	0.101	0.094	0.042	½ hour
D 7	0.126	0.155	0.145	0.136	0.129	0.029	½ hour
D 8	0.100	0.146	0.155	0.135	0.116	0.055	1 hour
D 9	0.105	0.110	0.128	0.120	0.110	0.023	1 hour
D10	0.100	0.147	0.140	0.114	0.099	0.047	½ hour
D11	0.110	0.149	0.141	0.139	0.110	0.039	½ hour
D12	0.095	0.160	0.150	0.100	0.100	0.065	½ hour
D13	0.125	0.130	0.148	0.144	0.140	0.023	1 hour
D14	0.108	0.116	0.108	0.120	0.104	0.018	2 hours
D15	0.112	0.120	0.151	0.140	0.120	0.039	1 hour
D16	0.100	0.165	0.150	0.125	0.102	0.055	½ hour
O17	0.100	0.148	0.134	0.122	0.103	0.048	½ hour
D18	0.105	0.130	0.125	0.110	0.105	0.025	½ hour
D19	0.110	0.128	0.147	0.160	0.110	0.040	2 hours
D20	0.135	0.163	0.142	0.120	0.131	0.028	½ hour
D21	0.124	0.146	0.183	0.180	0.146	0.059	1 hour
D22	0.127	0.136	0.160	0.175	0.120	0.052	2 hours
D23*	0.120	0.210	0.150	0.146	0.130	0.090	½ hour
D24*	0.100	0.160	0.175	0.145	0.085	0.075	1 hour
D25*	0.140	0.148	0.182	0.130	0.132	0.048	1 hour
Average	0.110	0.143	0.144	0.131	0.114	0.043	

* Females.

MATERIAL STUDIED

In all, 107 cases of mental disease were studied. Of this number, eighteen occurred in females. The mental diagnosis was made after a period of observation extending over several months. An effort was made to include cases that showed characteristic pictures. Of these 107 cases, 52 were diagnosed as dementia praecox, 17 as manic-depressive insanity, 7 as paresis and 3 as morphinism. The remaining 24 included feeblemindedness, epilepsy, alcoholism, involution melancholia, hyperthyroidism and a number of clinically obscure cases.

Our interest centered largely on the dementia praecox cases. The fifty-two cases in this group were subclassified into twenty-five hebephrenic, eleven catatonic, seven simple deteriorating and nine paranoid types.

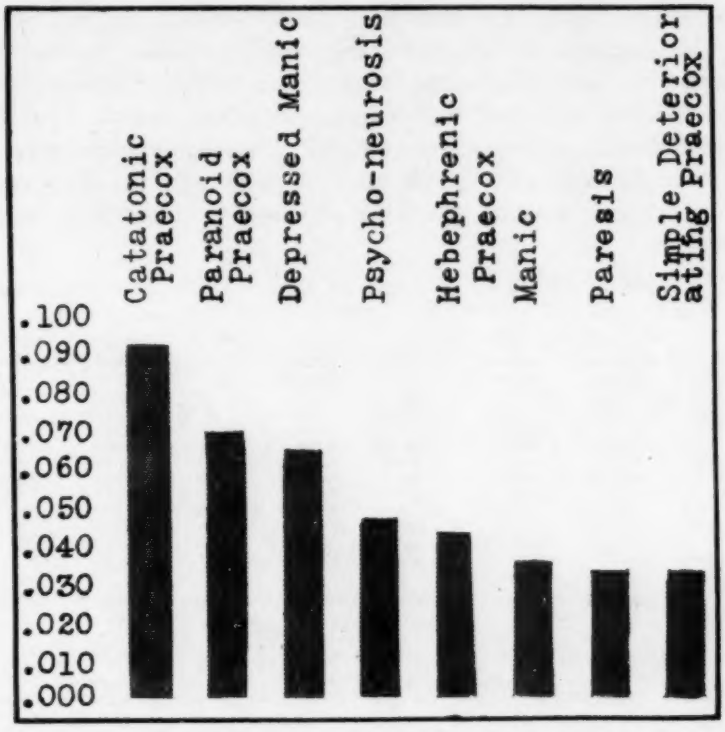

Chart 4.—Diagrammatic representation of average maximum rise of blood sugar in the various conditions noted. Horizontal line at .045 represents the average normal rise.

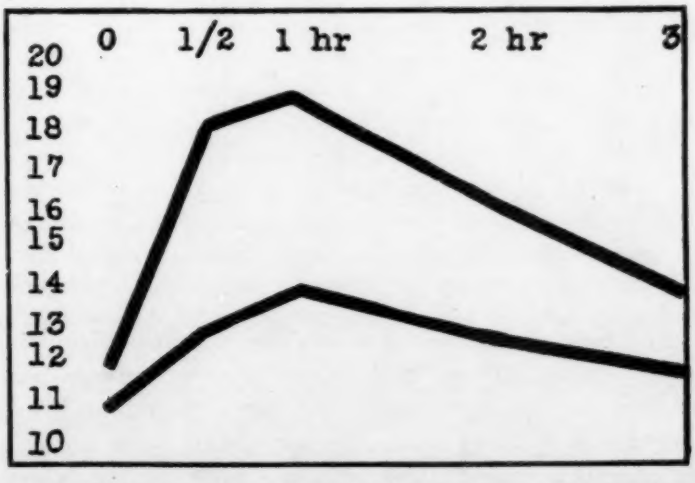

Chart 5.—The upper curve represents the average reaction in catatonic cases. The lower curve shows the average reaction in simple deteriorating dementia praecox.

DEMENTIA PRAECOX

The response to sugar feeding was practically normal in the hebephrenic type. The initial blood sugar concentration after a twelve hour fast was uniformly higher in the catatonic patients than in those with other forms of dementia praecox. The average initial level of the catatonic patients was 0.120 per cent. as compared to 0.110 per cent. for the hebephrenic patients and 0.108 per cent. for those with the simple

TABLE 2.—GLUCOSE TESTS IN CASES OF DEMENTIA PRAECOX, PARANOID TYPE

Case No.	Before Feeding	½ Hour Interval	1 Hour Interval	2 Hour Interval	3 Hour Interval	Total Rise	Period of Rise
P D 1	0.130	0.183	0.165	0.145	0.130	0.053	½ hour
P D 2	0.150	0.215	0.185	0.180	0.175	0.065	½ hour
P D 3	0.125	0.150	0.125	0.126	0.128	0.025	½ hour
P D 4	0.130	0.210	0.165	0.138	0.136	0.080	½ hour
P D 5	0.160	0.212	0.163	0.160	0.150	0.052	½ hour
P D 6	0.105	0.150	0.126	0.125	0.115	0.045	½ hour
P D 7	0.12	0.182	0.165	0.134	0.125	0.062	½ hour
	0.145	0.165	0.210	0.186	0.144	0.065	1 hour
P D 8*	0.11	0.135	0.130	0.115	0.115	0.025	½ hour
P D 9*	0.131	0.190	0.316	0.250	0.145	0.185	1 hour
Average	0.130	0.179	0.175	0.155	0.136	0.065	

* Females.

TABLE 3.—GLUCOSE TESTS IN CASES OF CATATONIC DEMENTIA PRAECOX

Case No.	Before Feeding	½ Hour Interval	1 Hour Interval	2 Hour Interval	3 Hour Interval	Total Rise	Period of Rise
C 1	0.118	0.218	0.140	0.130	0.121	0.100	½ hour
C 2	0.10	0.194	0.116	0.108	0.098	0.094	½ hour
	0.127	0.188	0.210	0.180	0.144	0.083	1 hour
C 3	0.065	0.166	0.131	0.121	0.100	0.071	½ hour
	0.12	0.185	0.245	0.252	0.24	0.132	2 hours
C 4	0.105	0.198	0.180	0.165	0.115	0.093	½ hour
	0.121	0.196	0.230	0.212	0.124	0.109	1 hour
	0.138	0.218	0.206	0.204	0.135	0.080	½ hour
C 5	0.108	0.166	0.214	0.165	0.106	0.106	1 hour
	0.142	0.215	0.230	0.185	0.170	0.088	1 hour
C 6	0.106	0.135	0.206	0.145	0.115	0.100	1 hour
	0.118	0.162	0.210	0.210	0.130	0.092	1 hour
C 7	0.140	0.265	0.220	0.165	0.142	0.125	½ hour
C 8	0.106	0.145	0.193	0.162	0.145	0.087	1 hour
C 9	0.118	0.152	0.195	0.146	0.134	0.077	1 hour
	0.121	0.152	0.192	0.140	0.126	0.071	1 hour
C10	0.120	0.160	0.135	0.125	0.115	0.040	½ hour
C11	0.110	0.140	0.13	0.12	0.12	0.030	½ hour
	0.130	0.160	0.255	0.224	0.15	0.125	1 hour
Average	0.118	0.179	0.191	0.166	0.133	0.089	

deteriorating type of disease. The average maximum rise of blood sugar following the glucose meal in the catatonic patients was over 0.20 per cent., in the hebephrenic 0.14 per cent. and in the simple deteriorating type 0.13 per cent. The increase of blood sugar for the catatonic patients averaged 0.094 per cent., while for the hebephrenic and simple deteriorating types the average was between 0.025 and 0.033 per cent.

The paranoid type, of which there were nine cases, also showed a reaction above normal. The average initial level was 0.130 per cent. The high point averaged 0.159 per cent., and the total increase above initial level averaged 0.046 per cent.

Of the dementia praecox group, therefore, the catatonic patients clearly showed an abnormal response that closely resembled the curve obtained in hyperthyroidism.

TABLE 4.—GLUCOSE TESTS IN CASES OF DEMENTIA PRAECOX, SIMPLE DETERIORATING TYPE

Case No.	Before Feeding	½ Hour Interval	1 Hour Interval	2 Hour Interval	3 Hour Interval	Total Rise	Period of Rise
S D 1	0.092	0.091	0.096	0.095	0.088	0.004	1 hour
	0.098	0.090	0.098	0.098	0.088	0.000	
S D 2	0.122	0.132	0.140	0.140	0.135	0.018	1 hour
S D 3	0.097	0.146	0.145	0.110	0.110	0.049	½ hour
S D 4	0.115	0.134	0.180	0.152	0.125	0.065	1 hour
S D 5	0.100	0.115	0.153	0.151	0.132	0.053	1 hour
S D 6	0.105	0.141	0.123	0.112	0.102	0.036	½ hour
S D 7	0.115	0.132	0.130	0.125	0.122	0.017	½ hour
Average	0.105	0.122	0.133	0.122	0.113	0.034	

TABLE 5.—GLUCOSE TESTS IN CASES OF PARESIS

Case No.	Before Feeding	½ Hour Interval	1 Hour Interval	2 Hour Interval	3 Hour Interval	Total Rise	Period of Rise
P 1	0.121	0.143	0.108	0.110	0.106	0.022	½ hour
P 2	0.094	0.105	0.130	0.105	0.10	0.036	1 hour
P 3	0.103	0.131	0.120	0.107	0.103	0.028	½ hour
P 4	0.086	0.127	0.130	0.110	0.098	0.044	1 hour
P 5	0.094	0.142	0.132	0.112	0.102	0.048	½ hour
P 6	0.113	0.151	0.130	0.117	0.111	0.038	½ hour
P 7	0.106	0.125	0.130	0.125	0.103	0.024	1 hour
Average	0.102	0.132	0.125	0.112	0.102	0.034	

PARESIS

Seven cases of paresis were included in this series. All responded in a strikingly similar manner, the uniformity of the curves being remarkable. The initial level in paresis was 0.101 per cent. The highest concentration after feeding varied from 0.110 to 0.151 per cent. The average for all cases was 0.132 per cent. At the end of the third hour in every case the blood sugar concentration closely approached the initial level. The increase above initial level averaged 0.033 per cent. The response in patients with paresis thus tends to be somewhat less than the normal.

MANIC-DEPRESSIVE INSANITY

Of this group, six males and four females were in a manic phase. The initial, fasting blood-sugar level ranged from 0.102 to 0.126 per cent. and averaged 0.111 per cent. The maximum rise occurred during the first hour and reached an average of 0.145 per cent. The increase above the initial level averaged 0.035 per cent. This response is less

than normal. The individual variation from the average response among these cases was not great.

Seven depressed cases were tested. The initial blood sugar level varied from 0.082 to 0.122 per cent., the average being 0.106 per cent. The maximum concentration after feeding occurred during the first hour and averaged 0.154 per cent. The increase was approximately 0.05 per cent., which is greater than the normal response. Our findings, therefore, tend to corroborate the observations reported by Kooy.[19]

TABLE 6.—GLUCOSE TESTS IN CASES OF MANIC-DEPRESSIVE INSANITY, MANIC PHASE

Case No.	Before Feeding	½ Hour Interval	1 Hour Interval	2 Hour Interval	3 Hour Interval	Total Rise	Period of Rise
				Males			
M 1	0.114	0.12	0.132	0.13	0.105	0 018	1 hour
M 2	0.10	0.14	0.132	0.105	0.092	0.04	½ hour
M 3	0.122	0.16	0.162	0.13	0.115	0.04	1 hour
M 4	0.112	0.158	0.14	0.132	0.12	0.046	½ hour
M 5	0.12	0.142	0.164	0.15	0.126	0.044	1 hour
M 6	0.104	0.13	0.15	0.125	0.112	0.046	1 hour
Average	0.112	0.141	0.146	0.128	0.111	0.039	
				Females			
M 7	0.11	0.133	0.144	0.13	0.112	0.034	1 hour
M 8	0.107	0.141	0.115	0.102	0.102	0.034	½ hour
M 9	0.102	0.142	0.135	0.115	0.096	0.04	½ hour
M10	0.126	0.157	0.153	0.136	0.128	0.031	½ hour
Average	0.111	0.143	0.136	0.120	0.109	0.034	

TABLE 7.—GLUCOSE TESTS IN CASES OF MANIC-DEPRESSIVE INSANITY, DEPRESSED PHASE

Case No.	Before Feeding	½ Hour Interval	1 Hour Interval	2 Hour Interval	3 Hour Interval	Total Rise	Period of Rise
M D 1	0.082	0.094	0.136	0.100	0.083	0.054	1 hour
M D 2	0.098	0.150	0.142	0.137	0.120	0.052	½ hour
M D 3	0.110	0.125	0.193	0.138	0.107	0.083	1 hour
M D 4	0.120	0.202	0.164	0.130	0.135	0.082	½ hour
M D 5	0.100	0.164	0.140	0.133	0.127	0.064	½ hour
M D 6	0.122	0.140	0.165	0.120	0.125	0.043	1 hour
M D 7	0.114	0.147	0.162	0.152	0.132	0.048	1 hour
Average	0.106	0.146	0.157	0.130	0.118	0.060	

PSYCHONEUROSIS

In this group there were five cases. The average initial blood sugar level was 0.108 per cent. The maximum concentration averaged 0.151 per cent. and the increase averaged 0.047 per cent. This response is approximately normal.

MORPHINISM

Three cases of morphinism are included in this series. The tests were made before drug withdrawal in two patients, T 1 and T 2, who had received one-half grain of morphin (0.03 gm.) on the evening previous

to the test. They were fairly comfortable in the morning and presented no withdrawal symptoms. These two patients responded to the sugar tests in a decidedly abnormal manner. The initial blood sugar concentration was 0.134 and 0.145 per cent. After the sugar meal the blood sugar concentration rose rapidly to a high level. At the one-half hour interval both showed a concentration well above 0.2 per cent. At the hour interval one patient showed 0.3 per cent. During the succeeding two hours the blood sugar fell rapidly but had not returned to its initial level at the end of the third hour. The increase above the initial level in case T 1 was 0.157 per cent. and in case T 2 0.093 per cent. The third case is of interest. At the time of the sugar meal this patient complained bitterly of withdrawal pains. No morphin was given. The initial blood sugar concentration was 0.175 per cent., which is extremely high. After the feeding the concentration did not change but maintained the initial high level for approximately two and one-half hours, and at the end of the third hour was slightly below it.

TABLE 8.—GLUCOSE TESTS IN CASES OF PSYCHONEUROSES

Case No.	Before Feeding	½ Hour Interval	1 Hour Interval	2 Hour Interval	3 Hour Interval	Total Rise	Period of Rise
P N 1	0.086	0.095	0.126	0.102	0.085	0.040	1 hour
P N 2	0.108	0.117	0.136	0.120	0.103	0.028	1 hour
P N 3	0.120	0.135	0.156	0.144	0.123	0.036	1 hour
P N 4	0.100	0.162	0.140	0.132	0.102	0.062	½ hour
P N 5	0.130	0.140	0.200	0.151	0.126	0.070	1 hour
Average	0.108	0.129	0.151	0.129	0.107	0.047	

TABLE 9.—GLUCOSE TESTS IN CASES OF MORPHINISM

Case No.	Before Feeding	½ Hour Interval	1 Hour Interval	2 Hour Interval	3 Hour Interval	Total Rise	Period of Rise
T 1	0.145	0.224	0.292	0.206	0.156	0.147	1 hour
T 2	0.134	0.215	0.227	0.215	0.194	0.093	1 hour
T 3	0.175	0.175	0.17	0.168	0.166	0.000	

UNCLASSIFIED AND OTHER MENTAL STATES

An additional twenty-five cases were included in our series. These comprised feeblemindedness, epilepsy, alcoholism, neurasthenia, psychasthenia and a number of clinically doubtful or undetermined cases. It is interesting that of the clinically doubtful cases, in three, in which catatonic dementia praecox was considered (U 11, U 14 and U 18), the response to the test resembled the curve obtained in the frankly catatonic cases, the increase in blood sugar being 0.075, 0.076 and 0.082 per cent., respectively.

DISCUSSION

A considerable number of our patients were tested on several occasions in the course of two or more months; in some cases three

tests were made. The curves obtained on repetition of the tests were strikingly similar. In several cases the parallelism was closely maintained throughout the entire period of three hours. In one case of catatonia, C 11, the first test showed the character of curve obtained in every catatonic case, with the exception of C 10. A second test on C 11, several months subsequent to the first, was practically normal. After the first test this patient improved very much, and at the time of

TABLE 10.—Glucose Test in Unclassified and Other Mental States

Case No.	Before Feeding	½ Hour Interval	1 Hour Interval	2 Hour Interval	3 Hour Interval	Total Rise	Period of Rise	Diagnosis and Remarks
U 1	0.128	0.144	0.152	0.131	0.126	0.024	1 hour	Constitutional inferiority
U 2	0.097	0.116	0.125	0.110	0.102	0.028	1 hour	Feebleminded
U 3	0.114	0.153	0.136	0.126	0.120	0.039	½ hour	Feebleminded
U 4	0.123	0.150	0.133	0.125	0.118	0.027	½ hour	Feebleminded
U 5	0.115	0.120	0.154	0.126	0.120	0.039	1 hour	Feebleminded epileptic
U 6	0.123	0.130	0.144	0.126	0.114	0.021	1 hour	Epileptic
U 7	0.125	0.080	0.118	0.148	0.100	0.023	2 hours	Epileptic
U 8	0.105	0.138	0.125	0.121	0.115	0.033	½ hour	Alcoholic deterioration
U 9	0.105	0.172	0.165	0.150	0.122	0.067	½ hour	Chronic alcoholism hallucinosis
U 10	0.106	0.173	0.125	0.111	0.108	0.067	½ hour	Chr. alcoholism paranoid
U 11	0.115	0.183	0.190	0.162	0.132	0.075	1 hour	Unclassified manic symptoms; catatonia suspected
U 12	0.140	0.163	0.212	0.165	0.135	0.072	1 hour	Atypical manic
U 13*	0.152	0.195	0.159	0.142	0.145	0.043	½ hour	Neurasthenia and hyperthyroidism
U 14	0.100	0.162	0.176	0.147	0.080	0.076	1 hour	Dementia praecox with manic symptoms, possibly catatonic
U 15	0.098	0.205	0.222	0.125	0.085	0.124	½ hour	Psychasthenia
	0.105	0.200	0.195	0.132	0.114	0.095	½ hour	
U 16	0.132	0.131	0.187	0.165	0.112	0.055	1 hour	Involution melancholia
U 17	0.125	0.173	0.135	0.126	0.118	0.048	½ hour	Unclassified, possibly depressive manic
U 18	0.124	0.140	0.206	0.140	0.132	0.082	1 hour	Dementia praecox, possibly catatonic
U 19	0.110	0.180	0.120	0.115	0.114	0.070	½ hour	Unclassified atypical manic
U 20	0.108	0.165	0.180	0.115	0.104	0.072	1 hour	Dementia praecox hebephrenic, doubtful
	0.110	0.176	0.180	0.120	0.115	0.070	1 hour	
U 21*	0.101	0.160	0.134	0.121	0.125	0.050	½ hour	Manic-depressive insanity, mixed type
U 22	0.124	0.135	0.176	0.160	0.111	0.052	1 hour	Unclassified questionable dementia praecox
U 23	0.112	0.166	0.121	0.115	0.106	0.054	½ hour	Dementia praecox hebephrenic questionable
	0.115	0.185	0.178	0.127	0.115	0.070	½ hour	
U 24	0.100	0.145	0.138	0.133	0.102	0.045	½ hour	Dementia praecox hebephrenic questionable
	0.104	0.152	0.176	0.155	0.118	0.072	1 hour	

* Females.

the second test was markedly better. He was up and about, talked quite readily, was interested in occupational work and expressed no false ideas, but he had no insight into his former condition.[22]

22. Raphael, T., and Parsons, I. P.: Blood Sugar Studies in Dementia Praecox and Manic-Depressive Insanity, Arch. Neurol. & Psychiat. **5**:687 (June) 1921. These authors reported, during the period of our investigations, conclusions similar to our own. They found an abnormal sugar tolerance curve in dementia praecox; the depressions gave a high curve and the manic excitements a low response. The number of cases studied by them did not permit conclusions as to types of reponse in the different subgroups of dementia praecox. The patient in Case 9 of their series gave a very high curve similar to that which we obtained in catatonia.

Owing to lack of cooperation, it was often difficult to collect specimens of urine. We were able, however, to obtain them in over 50 per cent. of our cases. Examinations for sugar were made on all of these specimens. The results were by no means uniform, and we were not able to prove the assertion that a blood sugar concentration of 0.17 per cent. is the threshold of elimination. Many of our patients had a blood concentration above 0.2 per cent. for periods of one hour and more and yet failed to show sugar in the urine.

Assuming that the curves noted in hyperthyroidism are directly the result of altered thyroid function or, secondarily, the expression of disturbance in the endocrine chain, the conclusion that endocrine imbalance exists in catatonia is warranted. Whether this manifestation is due to a primary disturbance of any member of the endocrine system or whether it is merely the expression of altered function due to some emotional state cannot be decided on this evidence.

One case strikingly demonstrates the effect of emotion during the application of the test. Case P. D. 9 was one of paranoid dementia praecox in which ideas of persecution, particularly of poison administration, the use of noxious gases and electricity, were dominant. Shortly after taking the sugar solution the patient expressed fear of a poisonous dose. Later, when the first blood sample was taken, he manifested marked fear; his face was very pale; there was profuse perspiration, rapid breathing and a general picture of great apprehension. In this case the blood sugar rose from an initial level of 0.132 to 0.195 per cent. within one-half hour after feeding and at the hour interval reached 0.318 per cent. Following this high concentration a rapid drop was noted. At the end of the second hour the blood sugar was 0.25 per cent. and at the end of three hours it was 0.145 per cent., only slightly above the initial level. This patient showed the highest response of any in our series. The case of morphinism, T 3, also bears on the effect of emotion on blood sugar. The feeding of glucose in this case caused no response in the blood sugar. In attempting to interpret the abnormal responses found in catatonic dementia praecox, one must hold in mind the possibility that emotional states may exist without being clearly evident. It, therefore, still leaves us in doubt. The possibility of the existence of considerable emotional tension in an active catatonic state with consequent sensitiveness of the suprarenals and thus the possibility of an oversupply of epinephrin and an upset of the endocrine balance, which might be manifested by abnormal reaction to sugar feeding, must be considered.

Another group of patients that tended to show a uniform character of response was that of the seven patients with cases diagnosed as dementia praecox—simple deteriorating type. This subgroup, as usually interpreted, includes cases in which general mental deterioration is

evident without strikingly bizarre ideas or attitudes. Three patients gave responses that clearly simulated the reactions obtained in patients with hypothyroidism and allied conditions of hypofunction. Case SD 1 showed, in two examinations, a blood sugar level that remained low throughout the test, the curve being almost a straight line. SD 2 and SD 7 gave slight responses, the maximum rise in blood sugar in each being less than 0.02 per cent. This group, taken as a whole, gave an average curve which is less than the normal response; the maximum rise was 0.025 per cent. In view of these findings one may suspect that, in some of these cases at least, there is an endocrine dysfunction.

CONCLUSIONS

1. Except in cases of active catatonia, certain cases of simple deteriorating dementia praecox and several cases in which evident emotional upsets existed at the time of the test, this investigation points to a blood sugar concentration in mental disease that is practically normal when the test is made while the patient is fasting, the average being 0.105 per cent.

2. The response of patients with mental cases, except the types mentioned in the foregoing, to sugar feeding is generally within normal range.

3. Patients with active cases of catatonic dementia praecox responded to glucose feeding with a hyperglycemia that resembles the response obtained in hyperthyroidism.

4. Several cases of simple deteriorating dementia praecox responded to glucose feeding in a manner that resembles the responses obtained in certain endocrine disturbances, such as dyspituitarism.

5. Patients with cases of manic-depressive insanity—depressed phase—responded to the sugar test with a curve higher than that found in normal subjects.

Abstracts from Current Literature

PHYSIOLOGY AND PATHOLOGY OF STEREOGNOSTIC AND SYMBOLIC PERCEPTION OF OBJECTS. G. SANTANGELO, Monatschr. f. Psychiat. u. Neurol. **49**:229 (April) 1921.

For a long time after Hoffman had introduced the term "stereognostic" into medical literature, the ability to recognize the form of objects was ascribed to a special sense called the stereognostic sense. It was later shown that no such special sense existed. Markowa pointed out that recognition of the shape of objects is a complex psychic act made up of peripheral and central components, so that instead of speaking of a stereognostic sense, we should speak of stereognostic perception.

Müller gives the following picture of the appreciation of form by touch: We receive certain impressions by touch and muscle sense; these awaken the memory of similar sensations, and call up a certain form which experience has taught us to associate with these sensations. This process is known as identification of the first order, between an immediate impression and the memory of a similar previous sensation. But Chretien points out that the process can go further. In addition to the identification of form, the sense perceptions can call up images whose elements are furnished from other sensory spheres—more especially the visual—and which give us all the characteristics of an object; in other words, we obtain the complete picture of the object, which permits us to recognize and name it. This process is called identification of the second order. We now use the term stereognostic perception for the tactile recognition of form, and symbolic perception for the tactile recognition of objects. Loss of these functions is termed astereognosis (failure of tactile recognition of form) and asymbolia (failure of tactile recognition of objects in spite of retention of adequate peripheral sensation).

There is considerable disagreement as to which modality of sensation is most important for the maintenance of stereognostic perception. There is still more disagreement regarding the mechanism of production of asymbolia. Wernicke, who was the first to call attention to asymbolia, believed that it results from the loss of tactile memory pictures. Later Flechsig and Monakow assumed an associative disturbance. According to them, asymbolia results from a break in the transcortical association paths between the true touch centers in the rolandic convolutions and the other sense centers, especially the visual. This would account for its frequent occurrence in parietal lobe lesions. According to Déjerine and his followers, symbolic disturbances cannot be explained by any such associative mechanism, but are the result of a summation of disturbances of peripheral sensation (always present, though slight) with general psychic disturbances, such as loss of attention, mental weakness, loss of memory, etc.

Recently Mochi has gone over all the cases in the literature. He verifies the associative nature of the disturbance and shows that it is localized generally along a line which connects the sensorimotor zone with the outer surface of the occipital lobe, about at the level of the middle third of the cerebral hemisphere.

The author has done experimental work in this field in several directions. First he attempted to determine the value of the various peripheral components which subserve the normal stereognostic function. His conclusions are:

Touch: Has scant significance in the appreciation of form.

Weber's Sense: (Compass test.) Important but not indispensable.

Temperature Sense: Loss of temperature sense disturbs to some extent the appreciation of form and the recognition of objects; its maintenance is of definite value in symbolic perception and of less value in perception of form.

Pain Sense: Little value.

Pressure Sense: Some importance.

The sense modalities described furnished no important contribution to stereognostic and symbolic perception. They give us more or less accurate data about the form of the surface; but neither one of them nor all together can enable us to recognize three dimensional forms and objects. The essential data for such recognition are furnished by muscle and joint sense, including sense of position, passive and active motion.

The author studied the stereognostic and symbolic functions of other parts of the body—sole, back, etc. With the sole he finds it possible to determine simple geometrical forms, but not to recognize objects. In the back conditions are similar but the response is slower. Whenever it is impossible to get an idea of the object in its entirety, symbolic recognition is impossible. He has attempted to use the stereognostic function for diagnostic purposes, more especially for accurate localization of cortical lesions of the rolandic zone. In such lesions we may find a loss of the stereognostic function of the hand, with retention of stereognostic function for the sole. A dissociation of this type can only occur in a lesion lying in, or immediately beneath, the rolandic cortex. In capsular or pericapsular lesions, owing to the crowding of the projection fibers, stereognostic function in hand and foot will be together.

Finally, the author points out that stereognostic perception is fully developed after the first year of life, and that physiologically there are no appreciable differences between right and left side in relation to perception of form and recognition of objects.

SELLING, Portland, Ore.

THE EFFERENT PATHWAYS OF THE EMINENTIA QUADRIGEMINA IN DOGS. A. BUSACCA, Ric. di morfol. **1**:261 (March) 1921.

Owing to the great discrepancies which still exist about the ascending projection tracts of the lamina quadrigemina, the author has undertaken special researches in mammals. In this paper he gives the results he obtained in dogs. Twenty-eight dogs were operated on by puncturing the lamina and killed from twenty to thirty days later. The central nervous system was then treated with the Marchi method. Protocols of nine cases in which the lesion was localized to the lamina quadrigemina are given. The remainder of the cases were omitted from the study, because the experimental lesion was not limited to the lamina alone. The author arrived at these conclusions:

In consequence of the lesion of the lamina quadrigemina in a dog, the following systems of fibers degenerate: tectospinal tract (crossed and uncrossed), tectoreticular fibers, commissural fibers between the superior colliculi, commissural fibers between the inferior colliculi and fibers in the brachium of the inferior colliculus.

The crossed tectospinal tract is constituted by a single bundle of fibers, whose cells of origin are situated in the various layers of the superior colliculi.

This tract circles around the central substance of the mesencephalon, passes through the fasciculus longitudinalis medialis and the red nucleus, and on the middle line crosses with the homologous tract of the opposite side along a line extending from the first roots of the oculomotor nerve to the caudal end of the red nucleus. Thence it goes to the mesencephalic half of the opposite side between the medial line, and the medial longitudinal fasciculus and the red nucleus. It bends caudally and after running before the medial longitudinal fasciculus reaches the rhombencephalon and the anterior portion of the anterior horn of the spinal cord. It may be followed as far as the cervical enlargement. This tract having its origin from the cells of the superior colliculi, must be considered as a reflex descending optic pathway intended to connect one of the primary optic centers to the underlying regions of the rhombencephalon and spinal cord.

The direct tectospinal tract is constituted by a single homolateral bundle which originates from the cells of the nucleus of the inferior colliculi and probably also from the cells of the other layers of this eminence. It runs first in the lateral lemniscus, then in the ventrolateral portion of the medulla oblongata and passes into the anterolateral portion of the anterior horn in the spinal cord (position of the olivospinal tract) where it can be followed as far as the level of the roots of the second pair of cervical nerves. This tract having its origin from the posterior eminence has the significance of a reflex descending acoustic pathway intended to connect one of the most conspicuous masses of gray substance, scattered along the course of the central acoustic pathway, with the underlying formations of the rhombencephalon and the spinal cord.

The anterior and posterior eminences are connected with the reticular formation of the mesencephalon by tectoreticular fibers which do not constitute a real bundle as it is maintained by some authors. These are disseminated fibers which go from the lamina quadrigemina to the reticular formation of the mesencephalon.

Between the anterior eminences, in their cephalic two-thirds, runs a system of fibers which cross posteriorly to the aqueduct of Sylvius and whose task it is to connect the two eminences. This system of fibers is in direct continuity with the posterior white commissure, which seems to receive also fibers from the superior colliculi. These fibers, however, do not reach the rhombencephalon.

The posterior eminences are interconnected by a system of fibers which is entirely independent from the one that unites the two anterior eminences. It also crosses behind the central gray substance of the aqueduct of Sylvius.

In the posterior eminences some fibers probably begin which, after entering the brachium of the inferior colliculus, go to the medial geniculate body. The author could not follow their degeneration beyond the nucleus of this geniculate body.

No degeneration was found in the brachium of the superior colliculus from a lesion of the superior colliculi. The author therefore is unable to confirm the existence of tectoretinal, tectothalamic and tecto-cortical fibers for Gudden's commissure admitted by some authors.

NACCARATI, New York.

RATING SCHEME FOR CONDUCT. JAMES S. PLANT, Am. J. Psychiat. **1**:547, 1922.

Plant presents an ingenious and interesting scheme for rating the conduct of mental patients. The field of inquiry is divided into physical and mental categories. Under the former are considered weight, sleep and physical exer-

cise, while under the latter is estimated attitude toward taking food, room and attire, reaction toward the nurses, care of self ("tidiness"), general knowledge as shown in conversation, emotional reaction, resourcefulness and ingenuity, rapidity of habit formation, span of attention, hallucinations, delusions, orientation, insight, recent memory, reaction to visitors, and judgment. The determinations are made by nurses who assign a rating value, usually from 1 to 10 in each subdivision. For instance, under "attention" a stuporous patient would be rated 1 while a patient who "plans and carries out a piece of work requiring a long period of time, as weaving a rug or making a piece of pottery," would be rated 10. Three calculations are made, constituting the average for the physical considerations, the average for the mental, and finally, the average for the standard deviation of the latter. The figures obtained are expressed graphically, and the status of the patient appears on the chart as a zone of varying width.

The author's idea possesses considerable merit. If further experience justifies the tentative conclusions that "where the average falls accompanied by a marked increase in the standard deviation" an ultimate recovery may be anticipated and where "a fall in the average accompanied by a marked diminution in the standard deviation" indicates chronicity, we will have a useful clinical prognostic guide. Again, the method calls for close observation and this in itself should exercise a favorable influence on the morale of the nursing force. In making deductions, there is necessarily a margin of error which must be borne in mind. This was reduced to a minimum in Plant's work largely because of his intimate and careful personal supervision. Failing this or some similar check, the usefulness of the plan would be seriously impaired, and it would be likely to degenerate into a more or less meaningless formula. Some clinicians may feel that the various categories should not be given equal weight. For instance, it might be pointed out that the affective far surpasses in importance most of the other reactions which are listed. However, practically it is true that it is impossible to deal with pure and separate subdivisions of conduct so that actually major symptoms give to minor ones their distinctive coloring and by enhancing their significance the proportionate balance of the rating value is maintained. This is particularly true of the emotional status so that in viewing the conduct from almost any angle we are perforce making some measurement of affect.

STRECKER, Philadelphia.

DISEASES OF PERIPHERAL NERVES. HARALD SIEVERT, Monatschr. f. Psychiat. u. Neurol. **49**:364 (June) 1921.

The author reports the results of a study of 393 cases of disease of the peripheral nerves. War injuries were excluded. The sciatic was the most frequently involved, 102 cases, or 26 per cent. of the total number. Bilateral involvement occurred in one case of severe sepsis. This fulfilled Heilbronner's dictum that a diagnosis of bilateral sciatica is justified only after complete recovery. The common causes mentioned are cold, alcohol and various infections. Gonorrhea was responsible for three cases. Pelvic sarcoma was responsible for four. By the time these four cases were recognized, the process was so advanced that the outlook was hopeless. In discussing therapy he emphasizes the use of hot air baths and hot sand bags in preference to moist heat. In severe cases epidural injection of a weak cocain solution in physiologic salt solution proved most valuable. "Vakzineurin" gave good results in the few cases of infectious origin in which it was tried. He states that in spite of

all skepticism, in spite of all search for other causative factors, we must still assign to "cold" a definite rôle in the etiology of sciatica.

Diseases of the trigeminal nerve were second in frequency. Involvement of the facial nerve is usually the result of "cold" or infection. A number of these cases, one of them bilateral, were syphilitic.

In musculospiral lesions (forty-three cases) alcohol and pressure paralysis (crutch paralysis) are important factors. Two cases in which the ulnar nerve was also involved resulted from the use of a tourniquet, and proved very resistant to treatment. Nicotin was responsible for one case, involving both musculospirals, the left median and the great occipital. Stopping tobacco resulted in relatively prompt recovery.

The ulnar nerve was involved in twenty-nine cases. In three it was bilateral, following pleurisy. He reports an interesting case of bilateral ulnar neuritis in typhus resulting in paresis and atrophy of the appropriate muscles and sensory loss. A week after discharge from the hospital, there had been no improvement. At this stage the patient developed typhoid fever and in the first phase of rising temperature there was marked improvement in function of the paretic ulnar muscles, accompanied by pain. After a week, the paresis dropped to its previous level, and the pain stopped. There was gradual recovery in the course of three months. In explaining this phenomenon the author suggests that the toxic materials liberated in the first week of the typhoid stimulated the diseased nerve fibers. He believes that the favorable action of "Vakzineurin" is attributable to the same cause. He emphasizes the favorable results which he has obtained by the use of "Vakzineurin," although he has apparently used it in relatively few cases. He recommends its further trial.

The author brings out a number of other points: That recovery in plexus lesions is slow; that true intercostal neuralgias are rare; that neuritis of the cutaneous femoris lateralis may occur in gout; that obturator neuritis may follow a severe cystitis. He reports three cases of neuralgia (?) of the glossopharyngeal nerve, all following angina. Symptoms consisted of severe, episodic pain in the pharynx and a cramp-like sensation there, and sensations radiating into the posterior portion of the tongue. The picture was identical in the three cases. He emphasizes the need of patience in these cases, on the part of both the physician and the patient.

SELLING, Portland, Ore.

STUDIES IN THE GROWTH AND DIFFERENTIATION OF THE TELENCEPHALON IN MAN. THE FISSURA HIPPOCAMPI.

MARION HINES, J. Comp. Neurol. **34**:73 (Feb. 15) 1922.

This is a very complete study of the morphogenesis and histogenesis of the hippocampal formation in human embryos from 11.8 mm. to 43 mm., with some observations on older specimens up to 85 mm. Most of this material is in excellent preservation, and the study of the carefully made wax models is supplemented by more complete histologic examination than has hitherto been attempted. The fissures described in the cerebrum of human embryos by previous workers are in some cases artefacts, in some cases transitory fissures, and in other cases fissures whose history can be traced through to the definitive adult pattern. Of the latter type, the first to appear is the arcuate fissure of His (which has no relation to the fissura prima of His appearing somewhat later); that this is the embryonic hippocampal fissure is demonstrated both by its morphology and by its relation to the underlying tissue differentiation, both of which are followed in the series of embryos to practically adult relations.

The hippocampal region can be recognized histologically before the 11.8 mm. stage, and from this age onward its characteristic structure is always visible. The hippocampal (arcuate) fissure appears at about 16 mm. The fascia dentata first appears at about 20 mm. as a marginal group of cells at the ventral border of the sulcus limitans hippocampi. These cells migrate dorsalward close to the pial surface in the ventral lip of the shallow hippocampal fissure, and at 85 mm. they begin to condense into the characteristic adult form.

The comparative anatomy of the hippocampus is reviewed, and the conclusion is reached that the reptilian hippocampal formation contains no fascia dentata. The structure so named by several comparative anatomists is hippocampal cortex, and the fissura arcuata of Herrick in reptiles is the hippocampal fissure, the early human condition running very closely parallel with that of reptiles. It may be added that the author's success in analyzing the development of this very difficult region was materially assisted by her familiarity with its comparative anatomy, for many details which have been overlooked or incorrectly interpreted by previous workers are intelligible only in the light of relations in lower vertebrates which are presumably ancestral.

C. J. Herrick, Chicago.

ON THE TOPOGRAPHY AND SIGNIFICANCE OF SOME BROWN SPOTS ON THE ABDOMEN OBSERVED IN CASES OF LUMBAR MYELITIS FROM POTT'S DISEASE. L. De Lisi, Arch. gen di neurol. psichiat. e psicanal. **2**:2 (Dec.) 1921.

The author reports four cases of spastic paraplegia from Pott's lumbar meningomyelitis in which he found a brown spot on the abdomen having a peculiar constant topographic distribution. He calls attention to the fact that such a spot has not been found in other spinal cord and vertebral diseases. The lower border of the brown spot extended between the two flexures of the groin. Its external margins were on the anterior ascellar line. The upper border reached the sixth rib except in one case in which the limit did not go beyond the lower third of the xipho-umbilical line. The spot occupied, therefore, the skin which received its spinal sensory innervation from the roots of the dorsal nerves—the fifth, sixth, seventh, eighth, ninth, tenth and eleventh nerves—but it was limited externally by a line corresponding to the division between anterior and posterior diramations of the perforating branches of the same dorsal nerves. The spot was of Addisonian nature. Two of the patients died; in one of them tuberculosis of the suprarenal capsules was found. The other patients showed clinical signs of frustre Addisonian disease, but necropsy examination could not be performed on the other who died.

The particular topography of the spot, situated within the territory of the roots and of the dorsal nerves which contract relationship with the ganglions of the lateral chain and with the communicating branches of the splanchnic system, suggests that the limited zone of pigmentation is the expression of a particular disturbance of the splanchnic solar system, maintained by a nervous and an endocrino-biochemical factor. There is no topographic relationship between the myelitis, which is localized beneath the real and the apparent origin of the splanchnic nerves, and the eventual lesion of the celiac-splanchnic system. The limitation of the spot to only one portion of the dermatoma (part of the anterior section) does not contrast with the funda-

mental biologic laws which govern the segmentary disposition of the pigmentation of the vertebrates and in general terms the segmentary disposition of the cutaneous sympathetic.

From the clinical and semeiotic point of view the described spot should be included in the category of the partial melanodermas which are usually encountered in the frustre Addisonism and in forms of tuberculosis; but it possesses indications of affection of a definite section of the sympathetic system.

Considering its nature and the high mortality already experienced in this small number of cases, its presence has a serious prognostic significance.

NACCARATI, New York.

A CASE OF TUMOR OF THE SPLENIUM OF THE CORPUS CALLOSUM. G. G. GUILLAIN, Ann. de méd. **11**:33 (Jan.) 1922.

This is a contribution to the semeiologic study of tumors of the corpus callosum and is based on observation of one case and a review of the literature.

A patient aged 52, in February, 1920, began to complain of headache and to show marked disturbance of memory. Early in the month of August, 1920, he entered the hospital with these symptoms: violent headaches; vertigenous sensations; no paralysis of any of the extremities or of any of the cranial nerves; no apparent alterations of sensibility; abolition of the deep reflexes of the legs; absence of superficial reflexes; a positive Kernig's sign; transitory urinary retention; unequal pupils with feeble reactions to light and on accommodation; severe mental symptoms with disorientation; amnesia and apraxia; subsequent blindness. The blood urea showed 52 mg. per hundred cubic centimeters. A lumbar puncture in September, 1920, gave a clear spinal fluid containing 48 mg. of albumin (rachialbuminimeter of Sicard), 6 lymphocytes per cubic millimeter, a negative Wassermann and a negative benzoin colloidal reaction. In October, when a (third) spinal puncture was performed, there were 7 cells, the Wassermann reaction was again negative, the benzoin colloidal test was negative in the syphilitic zone, but presented a slight curve in the meningitic zone (0000020002220000). But in addition there was now present a zanthochromia and an increase in pressure of the fluid, measuring 90 cm. of water (manometer of Claude). It had been impossible to estimate intracranial pressure by fundal examination.

The first symptoms had shown themselves in February, 1920. The patient died in October, 1920, an evolution relatively rapid for cerebral tumors. Necropsy examination confirmed the diagnosis of tumor of the splenium.

The author believes that there is a special symptomatology of tumors of the splenium, and he enumerates the symptoms as follows:

1. Signs of intracranial hypertension, with vomiting, headache and sometimes pupillary stasis. These signs are often less accentuated than in the other cerebral tumors.

2. Mental symptoms characterized by amnesia, bizarre acts and attitudes, emotional indifference, disorientation, sometimes by mental confusion, by torpor interrupted by periods of agitation and absence of a systematized delirium. In the late stage there is a veritable dementia. The mental symptoms have sometimes multiple resemblances to those of general paresis.

3. Frequent presence of paralyses, contractures and bilateral hypertonias. These effects appear to be due to the propagation of the neoplasm to the pyramidal fibers or central gray nuclei.

4. Possibility of phenomena of apraxia.

5. Absence of aphasia.

6. Habitual absence of paralyses of the cranial nerves of the base.

DAVIS, New York.

THE ORIGIN OF THE OTIC AND OPTIC PRIMORDIA IN MAN. G. W. BARTELMEZ, J. Comp. Neurol. **34**:201 (April 15) 1922.

This paper reports a part of the results of an extensive study of human development during the early part of the period of somite formation. It is based on twelve well preserved normal embryos ranging between three and sixteen somites. The most striking result here reported is the very early appearance of the otic primordium in embryos of two to three somites. Man is the only vertebrate so far recorded in which the otic plate is differentiated before the optic primordium. The otic plate first appears as a diffuse thickening of ectoderm in the hindbrain region. At four somites the acousticofacial ganglion appears and is clearly derived from the definitive neural tube.

Isolated thickenings (growth centers) of the cranial neural folds appear at a stage of seven to eight somites, which promptly fuse to form a continuous ridge, the "optic-crest primordium." An associated ventricular sulcus in the forebrain levels of the ridge indicates the position of the optic anlage. This is the earliest stage of this anlage which has been recognized in a mammal. The nonoptic part of this primordium proliferates mesectoderm and a large part of the trigeminal ganglion. This demonstration of the formation of mesectoderm from the neural tube is in line with the somewhat similar findings of Platt, Landacre, Stone, and others in Amphibia, and opens an important chapter in the histogenesis of the human head, the details of which remain to be filled in.

C. J. HERRICK, Chicago.

EARLY DIAGNOSIS AND TREATMENT OF DISSEMINATED SCLEROSIS. D. K. ADAMS, Brit. M. J. **2**:841 (Nov. 19) 1921.

This paper presents the findings of Adams and his collaborators, who studied a series of cases of disseminated sclerosis, clinically, serologically and experimentally. Clinically the author stresses the importance of transient disturbance of bladder function, of vision with diplopia and of fine nystagmoid movements as very early symptoms of the disease. Serologically he finds that the colloidal gold test is necessary in the diagnosis. Experimentally, fifteen rabbits were inoculated with spinal fluid from eight cases of multiple sclerosis and nine with blood from similar cases. Five of the first group and four of the latter developed definite nervous symptoms. Six additional rabbits were inoculated with brain and spinal cord emulsions from the rabbits showing nervous symptoms. Of these, two developed evidence of involvement of the nervous system. The author presents no definite conclusions as the results of these studies but seems rather to endeavor to confirm the hypothesis that multiple sclerosis is caused by bacteria. Adams advocates the administration of potassium iodid, mercury and arsenic in cases of dissemi-

nated sclerosis, the mercury to be given in the form of inunctions to toleration, the arsenic in the form of small repeated (up to twenty) doses of neo-arsphenamin intravenously, and the potassium iodid to be given by mouth.

POTTER, Mercer, Pa.

IRIDOCYCLITIS—PAROTITIS—POLYNEURITIS: A NEW CLINICAL SYNDROME. A. FEILING and G. VINER, J. Neurol. & Psychopath. **2**:353 (Feb.) 1922.

The main symptoms in the case history presented were: a prodromal stage of malaise with drowsiness and backache, right facial nerve palsy, two days later beginning iridocyclitis in the right eye and swelling, firm and painless, of the right parotid gland. About four days later the left facialis became weak; two days after this the left eye became involved, and swelling was observed in the left parotid.

When examined three weeks after the onset, a rash somewhat resembling an erythema nodosum was present on the anterior aspects of the legs and lower part of the thighs, leukopenia was present, the spinal fluid contained 15 lymphocytes per cubic millimeter, but there was no increase of globulin, and there was no fever. Cultural studies were negative. In addition to the swelling of the parotids, there were bilateral iridocyclitis and iridoplegia; both sides of the face were paralyzed, and there were signs of mild general polyneuritis.

During the next month the eye condition became worse and increased tension required repeated paracentesis. The paralyses and signs of polyneuritis gradually disappeared, and the parotitis cleared up. At the end of four months the patient had practically recovered.

Similar cases are adduced from the literature, and the authors, after discussing the relation to mumps, concluded that the syndrome is a clinical entity, distinct from mumps, but whether a specific infection or not is not known.

SINGER, Chicago.

SUTURE OF SEVERED MEDIAN NERVE WITH RAPID RECOVERY OF FUNCTION. EDGAR WIRTH, Brit. M. J. **2**:900 (Nov. 26) 1921.

After accidental section of the median nerve with complete loss of power in all the muscles and loss of epicritic, protopathic and deep sensibility in the area supplied by this nerve, Wirth, after ligating the brachial artery and vein, performed an immediate end to end suture. Fine chromicized catgut was used to bring about an exact adaptation of the ends of the nerve. Two days after the operation there was better flexion of the wrist, much better pronation of the forearm, less impairment in opposing the thumb and less difficulty in abduction of the thumb. At the end of six weeks the normal muscular power was almost restored, and there was little impairment of sensation. Trophic changes were noted in the skin of the thumb, index and middle finger, consisting of an exfoliation of the outer layers of the skin. After nearly five months there was slight difficulty in flexion of the terminal phalanx of the index finger and thumb. Epicritic and protopathic sensation were absent over the index finger only.

This case demonstrates the rate of recovery of a sectioned median nerve under the most promising conditions except for the impairment of the circulation resulting from ligature of the brachial artery.

POTTER, Mercer, Pa.

THE PHYLOGENETIC SIGNIFICANCE OF THE PLANTAR RESPONSE IN MAN. G. DE M. RUDOLF, J. Neurol. & Psychopath. **2**:337 (Feb.) 1922.

Observations of the movement of the big toe only in the plantar reflex in amphibia, reptilia, rodentia and carnivora gave either no response or a flexor one. In primates, including a chimpanzee, the responses were uniformly extensor. During the first two weeks of extra-uterine life many human infants gave a flexor response which usually became extensor a little later. One premature infant (30 weeks) gave no response. Some infants gave extensor responses within a few minutes of birth, and in some cases the adult flexor type of response appeared early.

The conclusion is drawn that, ontogentically, the plantar reflex in man passes through the phylogenetic stages of absent response, flexor, extensor and, finally, adult flexor response. This last stage is dependent on brain influence. In complete section of the cord a similar phylogenetic series is observed, absent response during the phase of spinal shock, flexor for a variable period and finally extensor. The adult flexion does not here reappear because brain control is not restored.

SINGER, Chicago.

DYSPITUITARISM: REPORT OF A CASE OF POSTERIOR LOBE INSUFFICIENCY CONTROLLED BY ORGANOTHERAPY. ROGER S. MORRIS and HIRAM B. WEISS, J. A. M. A. **78**:1522 (May 20) 1922.

The author reports a case of dyspituitarism in which the patient presented the picture of obesity, drowsiness, headache, frequent nocturnal urination, loss of sexual power and impairment of memory. These symptoms have been relieved and controlled over a period of six years by use of posterior lobe extract. Anterior pituitary extracts caused no improvement, and he had previously been given thyroid tablets with no change of symptoms except a loss of weight. Five years after beginning treatment with posterior lobe extract the blood sugar was 0.133 mg. per hundred cubic centimeters. A glucose tolerance test was given, and two hours after receiving the glucose the blood sugar was 0.239 mg. per hundred cubic centimeters. After six years' treatment with posterior lobe extract the sugar tolerance still remained low.

NIXON, Minneapolis.

THE RESULTS OF GONORRHEAL INFECTION OF THE NERVOUS SYSTEM. E. O'CONNOR, Quart. J. Med. **15**:69 (Oct.) 1921.

An extensive review of the literature on this subject leads the author to conclude that gonorrhea has a tendency to produce slight psychic manifestations which may be due to a feeble toxemia; that toxic delirium due to the gonococcus is rare; that gonorrheal cerebrospinal meningitis has been established clinically and confirmed microscopically; that gonorrheal meningomyelitis is rare.

POTTER, Mercer, Pa.

A COMPARATIVE STUDY OF THREE COLLOIDAL REACTIONS ON THE SPINAL FLUID. D. O. RIDDEL and R. M. STEWART, J. Neurol. & Psychopath. **2**:325 (Feb.) 1922.

Comparisons are here made between the results of tests with colloidal gold, gum mastic and benzoin solutions. In general paralysis the first and last gave

parallel results, the second did not agree so closely. Gold and mastic gave paretic curves with nonparetic fluids; benzoin did not. Syphilitic curves in nonsyphilitic cases were obtained with all three. Benzoin also often gave a slight precipitation in the middle tubes with normal fluids.

SINGER, Chicago.

EPILEPSY FROM THE PSYCHOLOGICAL STANDPOINT. A. CARVER, Brit. M. J. **2**:840 (Nov. 19) 1921.

This author believes that the epileptic syndrome results from a combination of psychologic, physiologic, anatomic and other factors. Carver says that each epileptic personality requires intensive individual study, that in the majority of cases the psychologic factors are by far the most important and an understanding of them is essential for therapeutic reasons.

POTTER, Mercer, Pa.

EXPERIMENTAL STUDIES ON THE HISTOGENESIS OF THE SYMPATHETIC NERVOUS SYSTEM. ALBERT KUNTZ, J. Comp. Neurol. **34**:1 (Feb. 15) 1922.

By operations performed on chick and frog embryos in stages preceding the differentiation of neuroblasts the neural crests were removed or the entire neural tube was removed for a number of postcephalic segments. In other cases, more or less of the ventral portion of the neural tube was destroyed, leaving the neural crests and the dorsal portion of the neural tube intact. In a fourth group an attempt was made to destroy the cells which give rise to the sensory ganglions of the vagi and the portions of the hindbrain from which the vagi arise. From the study of the sympathetic primordia of these operated embryos in later stages, it is concluded that the sympathetic primordia are made up of cells which arise from both the neural tube and the cerebrospinal ganglions. Those from the neural tube are far more numerous, and they arise in the intermediate portions of the walls of the tube, that is, in the region occupied by cell bodies of the preganglionic neurons of the adult. The fate of the cells which migrate into the sympathetic primordia from the neural crest was not determined. In the absence of spinal ganglions and dorsal nerve roots the efferent fibers of the spinal nerves are accompanied by cells of medullary origin, which are supposed to form neurilemma. The cells of the vagal sympathetic plexuses arise from the vagal ganglions and the walls of the hindbrain.

C. J. HERRICK, Chicago.

THE FREQUENCY OF MENTAL DISEASE BEFORE AND AFTER THE WAR. TOEPEL, Monatschr. f. Psychiat. u. Neurol. **49**:323 (June) 1921.

The author bases his conclusions on statistics furnished by the admissions to the Cologne Psychiatric Clinic in the year preceding the war (1913) and in the year following the war (1919). For statistical purposes he divides psychoses into exogenic, endogenic and psychogenic. Exogenic psychoses, which depend on damage to the body from without (traumas, toxins, bacteria) decrease or increase proportionately to the exciting cause. In the year following the war we would expect an increase of psychoses resulting from cranial

injuries and a decrease in the alcoholic psychoses. Endogenic psychoses, dependent on internal conditions and independent of external causes, should remain unchanged. Psychogenic disturbances which represent pathologic reactions to affective experiences should show a marked increase. The results of the statistical study are as follows: Cases of alcoholism markedly diminished; of schizophrenia moderately diminished; of epilepsy somewhat diminished; of mental deficiency, manic-depressive insanity and syphilitic psychoses, practically stationary; cases of hysterias, traumatic neuroses and psychopathic states greatly increased. The diminution in the number of cases of epilepsy coincides with Kluth's findings, and the author agrees with Kluth in attributing this diminution to the lessened alcohol consumption.

SELLING, Portland, Ore.

THE EARLY DEVELOPMENT OF THE CEREBRAL HEMISPHERES IN AMBLYSTOMA. H. SAXTON BURR, J. Comp. Neurol. **34**:277 (June 15) 1922.

Two themes are developed in this paper: 1. The fate of the neuropore is determined experimentally. In early larvae, before closure of the neuropore, a slight wound was made in its ventral lip and this was stained with Nile blue. The stained area could be followed throughout subsequent development, and it was found that the lamina terminalis is formed by the closure of the lateral lips of the neuropore, and the ventral lip of the latter becomes the terminal ridge of Johnston (locus of the future anterior commissure). Kingsbury's recent modification of the scheme of subdivision of the early neural tube proposed by His is confirmed. The floorplate of His ends in the fovea isthmi; the roofplate of His ends in the terminal ridge. Between these landmarks the lateral basal and alar laminae of His fuse in the midplane.

2. The method of evagination of the cerebral hemispheres is briefly described. It is concluded that the hemispheres are evaginated from alar laminae (of His) alone and in early stages show a tendency toward cephalocaudal lamination, on which in later stages is superposed the dorsoventral lamination described by Herrick in the adult.

C. J. HERRICK, Chicago.

INFUNDIBULAR POLYURIA. LHERMITTE, Ann. de méd. **11**:89 (Feb.) 1922.

In this extensive article which takes up the subject of diabetes insipidus and which is based on the study of a case with syphilitic etiology, Lhermitte reports that histologic study showed the existence of profound lesions which were confined to the infundibulum and tuber cinereum. The supra-optic, suprachiasmic and paraventricular nuclei were the nuclei of the latter which were so gravely concerned. In the infundibulum, nerve cell changes were associated with vasculomeningeal specific inflammation; but in the tuber cinereum, the lesion appeared purely cytologic.

Lhermitte stresses the point that the hypophysis was not the site of any histologic abnormality.

One main conclusion set forth affirms that diabetes insipidus does not rest on either a perversion or obliteration of an endocrinal secretion but is a disorder of renal secretion conditioned by central nervous system disease.

DAVIS, New York.

THE AUDITORY SENSE OF THE HONEY-BEE. N. E. McIndoo, J. Comp. Neurol. **34**:173 (April 15) 1922.

Bee keepers are agreed that bees can hear, yet they cannot prove it, and some critics still contend that it has never been experimentally proved that any insect can hear; nevertheless, within the last few years some good experimental results have been obtained. The author has examined all of the five organs of the honey-bee which have been alleged to serve this function, and he finds that none of them seem structurally adapted to serve as organs of hearing at all comparable with our own. In bees, some of these organs seem qualified to respond to vibrations, but in ways more nearly comparable with our organs of touch than with our organs of hearing.

C. J. Herrick, Chicago.

MAGNESIUM AS A SEDATIVE. Paul G. Weston, Am. J. Psychiat. **1**: 637, 1922.

Weston advocates magnesium sulphate as a sedative in disturbed mental states. Two hundred and fifty 1 to 2 c.c. injections of a 25 to 50 per cent. sterile solution of magnesium sulphate were administered to fifty patients, including a large number with agitated depressions. The usual result was relaxation and the production of sleep lasting from four to six hours. This method of chemical restraint is said to be devoid of danger, and in the event of untoward symptoms calcium chlorid (intravenously) will exert an immediate inhibitory effect.

Strecker, Philadelphia.

TASTE FIBERS AND THE CHORDA TYMPANI NERVE. J. M. D. Olmsted, J. Comp. Neurol. **34**:337 (June 15) 1922.

It has previously been shown that taste on the anterior part of the tongue is lost after severance of the chorda tympani and that taste buds of this region in the dog degenerate if the lingual nerve is cut distal to its junction with the chorda. To complete the demonstration of the course of these taste fibers, the chorda tympani and the lingual nerves were cut, in different dogs, proximal to their junction. In the first case, taste buds of the anterior part of the tongue degenerated; in the second case, the taste buds did not degenerate, thus confirming the central course of the taste fibers through the chorda rather than through the lingual branch of the fifth nerve.

C. J. Herrick, Chicago.

Society Transactions

PHILADELPHIA NEUROLOGICAL SOCIETY

March 24, 1922

N. S. YAWGER, M.D., *President, Pro Tem.*

SYPHILITIC PATIENTS SHOWING UNUSUAL FEATURES. DR. J. V KLAUDER.

A man, 38 years old, had had epileptiform seizures and crying spells. He was apprehensive, depressed and had memory and speech defects, pupillary abnormalities and exaggeration of the patellar reflexes. The blood Wassermann reaction was strongly positive and the spinal fluid typical of paresis. He also complained of precordial pain, palpitation and shortness of breath on slight exertion. Examination revealed aortic dilatation and insufficiency.

He was shown because he was an exception to the rule that patients with neurosyphilis rarely present clinical manifestations of tertiary syphilis elsewhere. Patients with a frank tertiary involvement of the skin, bones or viscera may present one or more neurologic abnormalities, but ordinarily the disease is expended in only one system of the body. The work of Warthin, however, indicates that this dogma is less true pathologically than it is clinically.

A man, aged 48, had had a chancre thirty years ago, but had not received treatment. He now has a cutaneous syphilid on the forehead, his only complaint. The pupils were unequal and irregular, and reacted sluggishly to light. The right knee jerk was feeble, the left absent. The blood Wassermann reaction was four plus; the spinal fluid showed 2 lymphocytes, a negative globulin reaction, colloidal gold 1110000000 and a negative Wassermann reaction in 1 c.c.

This patient, like the first, had tertiary syphilis with frank involvement of the nervous system, a normal spinal fluid and the absence of subjective symptoms of neurosyphilis. This type has been termed abortive, "burnt out" or imperfect tabes, and doubtless includes other forms of neurosyphilis. The presence of a normal spinal fluid in this class of patients, previously untreated, points to a spontaneous cessation of the underlying neurosyphilitic process. In these cases, the pupillary abnormality probably represents a "neurologic scar" of a former neuraxis involvement. It is generally believed, although not definitely established, that the spinal fluid is persistently positive for many years prior to the development of frank symptoms of neurosyphilis. Therefore, the presence of an isolated pupillary abnormality, in the type of case under discussion, together with a negative spinal fluid, does not warrant the belief that this objective symptom is a forerunner of tabes or some other neurosyphilitic process.

The statistics of Dreyfus are of importance in the discussion of such cases. He says that from 35 to 40 per cent. of patients with tertiary syphilis with isolated pupillary abnormalities have negative spinal fluids. Indeed, in his cases the spinal fluid remained negative after provocatory arsphenamin injections.

The significance of isolated pupillary abnormality in a syphilitic patient cannot be definitely stated until the spinal fluid is examined. This is important in the examination of syphilitic persons.

This woman, 31 years old; when three months pregnant, in April, 1920, suffered a complete right hemiplegia with aphasia and some impairment of audition. Her blood Wassermann reaction at that time was negative and the spinal fluid normal. Subsequent blood Wassermann tests showed moderately positive reactions. The spinal fluid remained normal.

Some years ago she gave birth to a dead infant. The placenta presented the appearance characteristic of syphilis, and the woman's blood Wassermann reaction at the time was four plus. She then received treatment with arsphenamin and mercury over a period of two years when the Wassermann reaction became negative, and several tests in the course of a few years were negative.

DISCUSSION

Dr. W. B. Cadwalader: Hemiplegia coming on during pregnancy or shortly after may be caused by embolism, quite independently of syphilitic infection. Dr. Ornsteen has recently reported such cases.

Dr. William G. Spiller: Hemiplegia developing in a syphilitic man should not be regarded as evidence of acute syphilis. Syphilis might leave the blood vessels highly diseased, and a rupture or thrombosis might occur later in a diseased vessel from other causes than acute syphilis.

Dr. Francis X. Dercum: I am firmly convinced of the existence of two strains of spirochetes. It is impossible to reconcile the symptoms of the exudative forms of syphilis with those of the parenchymatous form. It is a fact that in a large number of tabetic and paretic patients there is no history of an initial lesion or of a slight one. It may be asserted that sometimes the symptoms of both infections are present, and it is conceivable that infection with both strains of the spirochete may occur. The parenchymatous group, the so-called parasyphilitic group, occupies a place by itself. It is not at all unusual to obtain negative serologic findings in the parenchymatous group. They are cases which have immunized themselves for the time being. Any large clinic will present such patients as Dr. Klauder has shown. I regard changes in the pupil as the most important indication of syphilis. Slight irregularity, slight inequality or inequality in the reaction to light are indications that the pupils are developing into Argyll Robertson pupils.

THROMBOSIS OF THE ANTERIOR SPINAL ARTERY. Dr. A. M. Ornsteen.

Occlusion of the anterior spinal artery is not frequent and necropsies have been few. Spiller, in 1909, reported a case with softening from the fourth cervical to the second dorsal segment.

The anterior spinal artery, the last branch of the vertebral within the skull before it becomes the basilar, descends ventrad to the medulla and unites with its fellow of the opposite side at about the level of the foramen mangum, to form the anterior median spinal artery. The latter vessel descends the entire length of the cord in the anterior median fissure, being reenforced along its course by lateral branches entering through the intervertebral foramina from the vertebral, thoracic, lumbar and sacral vessels. The anterior spinal artery supplies the pyramids and the mesial fillet in the lower anterior portion of the bulb, and the upper few cervical segments of the cord through the first

portion of the anterior median spinal artery before the lateral anastomoses begin. In the cord, the gray matter and a portion of the anterolateral columns are nourished.

The syndrome to be expected from occlusion of these vessels is: spastic tetraplegia with disturbance of the sense of position and vibration because of pyramid and mesial fillet involvement. If the softening extends into the cervical segments, atrophy and fibrillary twitchings of segmental muscle groups occur in addition to the spastic tetraplegia. Disturbance in the recognition of pain and temperature may occur in a limited area from involvement of the central gray matter, or may be widespread below the lesion, unilateral or bilateral, depending on the amount of destruction of the anterolateral columns. I believe that the two cases herein reported are instances of thrombosis of the anterior spinal arteries.

The first patient, aged 54, a laborer, complained of stiffness in gait, weakness of the upper extremities and numbness in both hands and in the perineum. These symptoms began in November, 1921, when he suddenly felt his hands become numb; several hours later he experienced numbness in the lumbar region and left leg. On the next day, the numbness increased and was present in both arms and legs. On the third day others noticed that he was walking and bending peculiarly, and he felt increasing weakness and stiffness in both lower extremities. He continued to work for two days, but with great difficulty because of stiffness in arms and legs. On the fifth day while walking he fell to his kness, and with difficulty arose and managed to walk home. Improvement began about a week later. Three weeks after the onset he complained of numbness of both hands and forearms, of a feeling of warmth over the chest and abdomen, a sticking sensation around the genitals and perineum and infrequency and hesitancy of urination.

Examination showed a spastic gait with marked swaying in the Romberg position. The lower limbs were very hypertonic. The knee jerks were markedly exaggerated with bilateral patellar clonus. The ankle jerks were greatly increased; no clonus was present. There was a Babinski sign on the right. The abdominal reflexes were absent. The upper extremities were not notably hypertonic but the movements were slow and stiff, with fair power. The left biceps reflex was prompt, the right diminished; the triceps reflexes were greatly exaggerated. The right deltoid, suprascapular and infrascapular muscles were atrophied; the right triceps was not perceptibly atrophic but fibrillary twitchings were evident in this muscle and in the right biceps and deltoid. The sense of position was impaired in the toes of both feet, but not in the hands; vibration was not perceived in the feet, momentarily over the tibiae, and almost normally in the knees and hands. Tactile, pain and temperature sensations were undisturbed, although he made more mistakes in discerning temperature in the right forearm than in the other forms of sensation. Examination revealed atrophy of the left shoulder girdle with fibrillary twitchings in the infrascapular and triceps muscles.

The blood Wassermann reaction was negative. The blood pressure was: systolic, 160, diastolic, 90.

The second patient was a woman, 24 years of age, who on May 29, 1918, became tetraplegic in an hour and a half. For several weeks before the onset she complained of dull pain in the upper dorsal region. When walking upstairs, there was a stiff and drawing sensation in this area. Three days before the paralysis her neck felt heavy and stiff. On the morning of the day of onset she felt nothing unusual and in the afternoon she went out for a

walk. When she had walked about two blocks, a sudden sharp pain was felt in the cervico-thoracic spine radiating into the substernal region, accompanied by a numb sensation in both legs. She hurried home unaided, the numbness spreading to trunk and arms, especially the left. She was able to enter the house but had to be carried upstairs. Sharp sticking pains were felt throughout the entire body from the neck down; the fourth and fifth fingers of the left hand became spasmodically flexed; the lower extremities became stiff and in about an hour and a half she was completely paralyzed in all four extremities. The whole body felt numb; there was retention of urine for twenty-four hours. For eight weeks she had to be catheterized and there was obstipation. After three months power began to return in the right arm and then in the left, and in about eight months she was able to get about with the aid of two canes.

She now has marked spastic paraplegia, with adductor spasm, exaggerated patellar reflexes, double ankle clonus and a Babinski sign. The abdominal reflexes are absent. Motor power in the right upper extremity is fair; poor in the left. The small muscles of the left hand and those of the flexor surface of the left forearm are atrophied; the fourth and fifth fingers of this hand are contractured. The left supinator reflex is absent, but is active on the right. The biceps reflexes are prompt, more so on the right; the triceps reflexes are both exaggerated. No atrophy is seen above the elbows. The sense of position and vibration and stereognostic perception are normal in all extremities. Tactile sense is normal on the right and hyperesthetic on the left up to the eighth dorsal segment. Pain sense is notably diminished in the right leg and trunk up to the fourth dorsal segment and is normal in the upper extremities. Temperature sense is disturbed in both lower extremities, more marked in the right; cold causes a somewhat painful sensation in the left leg and is normal in each upper extremity. The pupils are normal. Serologic examinations and roentgenograms of the vertebrae are negative.

In this case the lesion appears to involve the anterior median artery to a rather low level in the cervical cord, seventh and eighth segments. There is no evidence of sympathetic paralysis. This patient was seen in the early days of her affliction by a number of eminent European neurologists; their diagnoses were as follows: Flatau and Goldflam of Warsaw and Fleishman of Kiev diagnosed the condition as "sclerosis" (of what character I do not know); the former gave her four injections of arsphenamin. Lapinsky of Kiev diagnosed a hemorrhage, whether hematomyelia or a subdural hemorrhage I cannot say. Cassirer of Berlin diagnosed hemotamyelia.

DISCUSSION

Dr. Daniel J. McCarthy: Could not a myelitis, meningomyelitis or hemorrhagic meningeal condition in the cervical cord itself explain these symptoms?

Dr. A. M. Ornsteen: A meningomyelitis with hemorrhage could explain all the symptoms, but the preservation of motor power for one and a half hours from the onset is against hemorrhage. In order to obtain a spastic upper motor neuron tetraplegia the lesion must be in the uppermost part of the cord in order to involve both pyramidal tracts. A hemorrhage usually produces paralysis suddenly, of a flaccid type at the onset; but here, at the time of the paralysis, the patient's limbs all became stiff. There was a contracture of the left hand and an extension stiffness of both of her extremities; an hour

and a half elapsing between the onset of the initial symptoms and complete paralysis is in favor of thrombosis, which might be secondary to meningomyelitis rather than hemorrhage into the gray matter of the cord. If the posterior spinal artery is affected the anterior horns are not involved.

THE THALAMIC SYNDROME. Dr. N. W. Winkelman.

This patient, 70 years old, was fairly well until fourteen months ago, when, as he was walking, things suddenly became black in front of him, and he fell to the ground. He was not unconscious, but was dazed and after a few minutes was able to walk a short distance to his home. He was in bed for a day or two. So far as could be determined, there was no aphasia or paralysis, though there was weakness on the right side of the body, including the face. About four or five months after this attack he began to have pain over the entire right side of the body; at first very mild, gradually increasing in intensity, until now he finds it almost unbearable. Sometimes it feels as if the entire right side were burning and at other times it feels very cold. On the right side there is a feeling as if a phonograph were playing.

Examination revealed a short, well developed, man, who was emotional, and cried easily. His teeth were in poor condition, and he had marked arteriosclerosis. His blood pressure was: systolic, 195; diastolic, 100; his heart was much enlarged; there was a loud mitral systolic murmur and marked edema of the ankles. When touched lightly on the right side he complained bitterly of pain. He walked rather stiffly and dragged the right leg a little, holding the right arm as if afraid to touch anything with it. Fine movements of the fingers were well performed on both sides. The pupils were small, slightly irregular but reacted normally, and the cranial nerves were normal. The reflexes were a little more prompt on the right and there was slight weakness on that side but no ankle clonus or Babinski sign. There was hypesthesia on the right, more marked distally. When touched on the right side with the point of a pin or with hot or cold tubes he complained of severe pain over the entire right side, but this also was more marked distally. There was distinct impairment of the vibratory sense and the sense of position in the right lower extremity. There was no astereognosis. There were no visual disturbances and no choreic or athetoid movements. He showed a senile type of mental change.

I would ask the question which Souques asked Lhermitte when the latter presented a case of thalamic disease at the Paris Neurological Society; namely, whether the thalamus is always at fault in a case of this kind or whether a lesion of the parietal region or of the fasciculus thalamocorticalis cannot produce the same syndrome.

DISCUSSION

Dr. Charles K. Mills: I have seen the same or a very similar syndrome, including even the dysesthesia supposed to be pathognomonic of thalamic disease, in a case of lesion of the parietal lobe between the thalamus and the cortex, demonstrated at necropsy. Such a lesion would of course involve the tracts of communication both from the thalamus to the cortex and from the cortex to the thalamus. It is probable that the nearer the lesion reaches the thalamic border the more likely will the symptomatology approach that of true thalamic disease. I am not sure also that we may not have a syndrome closely approximating that of Dr. Winkelman's case from a tegmental lesion below, but not far removed from the thalamic entrance zone.

Dr. F. X. Dercum: Dr. Mills' view that the lesion might be above the thalamus hardly applies in the present instance because of the absence of astereognosis. If the lesion were in the corticothalamic fibers, astereognosis in some degree would have to be present. I do not think that we can escape from the conclusion that in this case the lesion is in the thalamus.

Dr. W. G. Spiller: I should like to have satisfactory evidence that a lesion entirely below the optic thalamus may cause spontaneous pain in one half of the body. Gordon Holmes has spoken of central pain from lesions of the spinal cord, but I am unable to refer to any reliable case in which a lesion entirely subthalamic had caused intense unilateral pain, affecting both upper and lower limbs.

HISTOLOGIC CHANGES PRODUCED EXPERIMENTALLY IN THE CENTRAL NERVOUS SYSTEM OF MONKEYS BY MERCURY.

Drs. Baldwin Lucke and John A. Kolmer.

In previous papers on the histologic changes produced in rabbits and rats by arsphenamin, neo-arsphenamin and mercury we have reported certain lesions in the central nervous system which may be summarized as follows: Multiple doses of the arsenicals, in excess of the calculated therapeutic amounts, produced hyperemia, focal hemorrhages, some endothelial proliferation and frequently hyaline thrombosis. After multiple doses of the mercurials, the most striking findings in a considerable number of rabbits were perivascular and pial small round cell infiltration. This latter lesion had not been observed in the numerous control animals, nor in those treated with the arsenicals, and was therefore regarded as being induced by the mercurials used. We felt, however, that these experiments should be repeated, and we selected monkeys because of their closer phylogenetic relationship. An added reason for this selection was that spontaneous lesions in the various organs of the rabbit are of not infrequent occurrence.

Histopathologic study of the brains from three monkeys treated for a period of three months by intramuscular injection and inunction, respectively, of different mercurials revealed a number of distinct tissue changes which may be summarized as follows: 1. The pia arachnoid was locally thickened and cellular. This was most pronounced in the sulci and was chiefly due to fibroblastic hyperplasia. 2. The endothelium of many capillaries and of the small vessels in general was large and swollen and in a state of active proliferation. New vessel formation, as evidenced by capillary budding, was frequently observed. 3. Mild infiltration of the adventitial lymph spaces of the smallest vessels with lymphocytes, plasma cells and intermediate forms, was present. 4. There was a moderate proliferation of the cellular as well as of the fiber-forming neuroglia. The former was most distinct about proliferating capillaries, in the white matter and in the neighborhood of diseased ganglion cells; the latter was best seen in the subependymal and the marginal cortical layers. 5. A relatively small number of ganglion cells were in a state of acute degeneration. 6. The distribution of lesions mentioned was irregular, mainly local, and on the whole most pronounced in the basal portions of the brain.

Conclusions.—1. Mercury, administered over a period of three months in monkeys causes proliferative, degenerative and slight exudative changes in the central nervous system.

2. It is suggested that this investigation is applicable to the problem of human neurosyphilis.

DISCUSSION

DR. D. J. MCCARTHY: In the early use of arsphenamin there were some cases of overdosing, more particularly in children. Some cases of lead poisoning both human and experimental were reported from the Pepper Laboratory showing encephalitis. It appears to me that the dose of mercury per kilo is markedly larger than that we give to human beings. I should be amazed to find that lesions of paresis were due to mercury.

DR. F. X. DERCUM: I think the impression left in our minds is that we should use the metals in the treatment of syphilis with caution. It opens up also the greater question, not yet settled, as to other effective methods of treating syphilis. A great many things can perhaps be developed by a more intensive study of the biology of the spirochete.

DR. SHERMAN F. GILPIN: The practical fact in regard to paresis or tabes is that many of the patients do not know they have had syphilis, and have never received mercury or arsenic. The animals used in these experiments did not have syphilis. The person who is nonsyphilitic and who takes mercury in a very small dose soon has marked local manifestations in the mouth and intestines. I do not see how we can judge the effect of mercury or arsenic on syphilitic persons by the effect of mercury or arsenic on nonsyphilitic animals.

DR. ALFRED GORDON: The statements of Drs. Lucke and Kolmer appear to be revolutionary. How will they explain cases with removal of acute symptoms after mercurial treatment? It would be very interesting to hear Dr. Kolmer explain this apparent paradox. It is discouraging to witness a condemnation of the well tried drug. How long did the treatment of monkeys continue, and what was the amount of mercury given in comparison with similar treatment in man?

DR. W. B. CADWALADER: I have occasionally noted diminution of vigor in syphilitic patients after unusually prolonged and intensive treatment with mercury and arsenic; a depression of vital functions which might have been caused by the drugs, not by syphilis. Has Dr. Lucke, in his experimental animals, observed anything that might correspond to this condition?

DR. JOHN A. KOLMER: The dose of mercuric salicylate administered to these animals by intramuscular injection corresponded to 1 grain (0.06 gm.) per 60 kilos of body weight. The inunctions were administered in the form of blue ointment in doses of 1 dram (3.9 gm.) per 60 kilos. Theses amounts correspond to those ordinarily administered to human beings in the treatment of syphilis.

Both Dr. Lucke and myself desire to say that we do not regard these histologic changes of sufficient degree to influence unfavorably the treatment of syphilis with mercury. The changes were largely intravascular and well within the range of repair. Therefore, while they may occur in the human brain in cases of syphilis intensively treated with mercury, they probably do not produce permanent injury or symptoms. However, answering Dr. Cadwalader, our animals lost considerably in weight and showed the effects of mercurialization.

Dr. Lucke and myself do not regard these lesions as likely to be mistaken for the histologic changes found in paresis; we simply believe that we have data showing that the administration of mercury to lower animals may produce lesions which are somewhat similar to some of the changes in paresis. *Spirochaeta pallida* induces lymphocytic infiltration in practically all tissues in which it may be located, and we believe that it is interesting to learn that the

administration of mercury may result in the production of areas of lymphocytic infiltration and endothelial changes of a similar kind and probably caused by the deposition of mercury in these tissues.

DR. BALDWIN LUCKE: Treatments for three months with any drug in therapeutic doses cannot produce the same lesions as disease that has lasted for many years. This ought to be understood. If I had treated these animals for three years, or ten years, the story might have been entirely different. I know that relatively small quantities of any of the metallic salts will produce profound changes in the liver and kidneys and elsewhere; there is no reason to expect that the brain would be exempt. We are not asserting that mercury causes paresis or tabes; we are simply stating that in these monkeys, treated for a relatively short time, there occurred certain changes in the nervous system that simulated in part the early changes in paresis.

THE DIAGNOSIS OF BRAIN TUMORS BY THE BÁRÁNY TEST, WITH REPORTS OF CASES PROVED BY OPERATION OR NECROPSY. DR. LEWIS FISHER.

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CONCLUSIONS

1. In cases of cerebellopontile angle lesion the Bárány tests are absolute. By means of them these lesions can be definitely located or excluded long before the appearance of the ordinary clinical findings.

2. Lesions of the posterior fossa generally give fairly constant findings in the Bárány tests. I believe that they are of great value in the differential diagnosis between a subtentorial or supratentorial lesion.

3. The Bárány tests are also helpful to a lesser degree in lesions in the middle or anterior fossa.

DISCUSSION

DR. J. HENDRIE LLOYD: The most satisfactory experience I have had with the Bárány tests has been in syphilis of the eighth nerve. Dr. Fisher made some of these examinations for me, and it was very interesting to observe the abolition of the nystagmoid movements and of the vertigo. The Bárány tests are intended simply to test the functions of the vestibular nerve. That is all they can do. In some of these cases in which there is paralysis of the eighth nerve, together with paralysis of the sixth and seventh nerves, there are good reasons for making a diagnosis without the Bárány tests, and in these cases we should not give too much credit to the Bárány test in making a diagnosis. But there are other cases. Two weeks ago I was present at a brain operation. The patient had been taken with very severe headaches following trauma, with very rapid onset of papilledema, progressing rapidly to blindness. There were practically no localizing symptoms. The woman was not deaf, she had no involvement of any cranial nerve except the second. She had an unsteady gait, not marked. The ophthalmologist and I thought she had a right lateral homonymous hemianopsia. There was such a high grade of papilledema that neither of us wished to attach too much importance to the changes in the visual field. She had also slight astereognosis of the right hand. The Bárány tests were made, and a lesion of the right cerebellum, in the right semilunar lobe, was diagnosed. The surgeon performed an exploratory and decompressive operation at that point, but found nothing. I believe that we shall be thrown off the track if we are not extremely careful. The trouble is that in some of

these examinations the otologist goes too far. He attempts to make a diagnosis. He hands it out to us and expects us to accept it. We do not do this in the case of any other cranial nerve, not even the optic nerves; why, then, should we attach such diagnostic importance to the vestibular nerve? In the case mentioned, the hemianopia and astereognosis probably indicated a lesion of the left parieto-occipital region.

Dr. William G. Spiller: Dr. Fisher has been of much assistance to me in the diagnosis of tumor of the cerebellopontile angle by means of the Bárány tests. In two cases I did not consider the findings sufficient for a diagnosis of this condition, and yet Dr. Fisher had concluded from these tests that the tumor was situated in the angle, and he was correct. I have come to place much reliance on the diagnostic findings by the Bárány tests as related to angle tumors. I am not prepared to make any statement regarding the use of these tests in the diagnosis of tumors elsewhere.

It is surprising that the symptoms of angle tumor may be obscure, but cases occur in which the diagnosis of such a tumor from the clinical findings is extremely difficult, even when the tumor is of considerable size. It is therefore of the greatest importance that the Bárány tests are valuable in such cases.

Dr. Lewis Fisher: I think Dr. Lloyd's criticism timely and justifiable. I do not know who the otologist was in this case, but if he had had much experience in this work he would not have been so positive of the tumor in the semilunar lobe. Unfortunately this sort of diagnosis is made only too frequently by the inexperienced who have not seen a sufficiently large number of cases to have learned to evaluate certain things. It is no more than natural that this kind of hasty and unjustifiable diagnosis should work a great deal of harm in the development of this work. Up to the present state of our knowledge, I feel that the only lesion in which we are justified in making a positive diagnosis is one in the cerebellopontile angle. These tests should be only corroborative and suggestive, but never positive of lesions elsewhere.

I fear that I am unable to answer the question as to the percentage of failures. These were more frequent years ago when we thought we knew a great deal about this work but in reality knew very little. I do not recall a single failure in the case of a cerebellopontile angle tumor within the last five years. The results in operative cases are frequently misleading. For instance, in a case examined recently in a western city, I made a diagnosis of a cerebellopontile angle tumor. The doctor at whose request I saw the patient wrote me a week later that at operation, in spite of a big exposure, digital exploration failed to show the tumor. Because of free bleeding the operation had to be discontinued. I received another letter from him a week later, stating that the patient died and necropsy revealed a large tumor in the angle. I have come to regard, therefore, an operative finding as conclusive only where it is positive.

PHILADELPHIA PSYCHIATRIC SOCIETY

Stated Meeting, May 12, 1922

Albert C. Buckley, M.D., *President*

THE ORIGIN OF SPIRITUALISM. Dr. Charles W. Burr.

Long before recorded history, long before man could write, it was possible though unprovable that spiritualism existed. Its vogue in savage races of today is proof that it is a belief which would be sympathetic to the primitive

mind, unless one accepted the hypothesis that all savage races of today are degenerate descendants of higher ancestors. While this might be true of a few races, for example, in certain African tribes, it is not true of all. Some are simply races whose protoplasm has been able to ascend only to a certain stage, and then has stood still. At all events, in every savage race today in Africa, Australasia, Asia, South America and the land of the Esquimaux, spiritism exists. Among the savages it has been accepted by the whole tribe; there are no skeptics. It is only in civilized man that we find any, let alone a majority, who refuse to accept it. If truth were proved by majorities contrary to fact, then spiritualism was proved to be true milleniums ago.

Dr. Burr summed up the facts about primitive man: Assume that he had developed so far as to live as a family. He was a herding animal, and it was only thousands of years later that he lived in tribes. He and his woman and offspring lived together permanently. The era of casual breeding had passed. He had learned that he must fight for his existence by cunning because many of his enemies exceeded him in strength. He had learned that sticks and stones were useful weapons; he had even learned that certain stones by flaking made better arms. Tools, with the exception of flints, he had none, nor did he need them except in the making of his flints. He had not become a cultivator of the ground. He might have become a fisherman. It would have been detrimental to him if he had, because he was overfed and lazy, and the hunter could easily beat him in any combat. He lived a precarious life, sometimes gorged, sometimes starved. Probably already infectious diseases had begun to take their toll. He was strong and hard-muscled; we have the proof of that in the big ridges on his bones where the muscles were inserted. He was not very tall. His jaws were strong, his teeth large, and his brows beetling. He was not beautiful to look at, but he was healthy. There were no weaklings, for it was probable that the diseases which lead to degeneracy had not arisen, and because a kindly nature, not restrained by the brutal sentimentalism of civilization, killed off all the accidentally unfit. He had inherited epilepsy from his mammalian ancestors, and probably mania from the anthropoids. Mentally, his memory was well developed, and his senses, especially sight and hearing, were acute. Taste and smell were probably little developed, or rather smell may have begun to decrease even in his anthropoid ancestors. Taste was of little value to him, because food was eaten not to tickle the palate but to feed the fires of his engine. His sense of physical pain was not acute. Sensations were developing into emotions. He already had a somewhat higher feeling toward his woman than had the ape. He had no sense of awe, no real esthetic pleasure. Fear was his great emotion.

Can we form a mental picture of primitive man, showing what his mental state was and decide whether or not he could have and would have developed ideas concerning communication with the dead?

First, Dr. Burr said, he wished to give an hypothesis concerning which mental qualities man inherited from his animal ancestors and which, if any, were peculiar to him. Dr. Burr, of course, accepted the theory of evolution, that is, the theory that there is an unbroken family line from man to the earliest form of living matter, whatever might be the method of introduction of anatomic and functional change in the formation of new species. For our purpose we are interested only in the mental side of racial inheritance. Which mental faculties did early man inherit from his ancestors? All of them. But the power of reasoning—that is, the ability, given any premise, to form a

judgment as to the consequences—was present in even the highest animals in only fragmentary form. Man's emotional nature, on the contrary, found almost its counterpart in many animals. Fear, pain, pleasure, love of a kind, man received from his humbler relatives. Memory also came from the same source.

His vocabulary was small because the subjects of his thoughts were few. Fear was his greatest emotion. The unknown and the unexpected terrorized him. Thunder and lightning, the avalanche, fire, great rivers, especially when in flood, and all the wondrous things, caused in him not awe and admiration, but abject terror.

He, during centuries or milleniums, developed mentally, and finally there arose what we today call the spirit of inquiry—he wanted to know the causes of things. He now had acquired the sense of awe. He dreamed, and being logical but having no education, no scientific tradition to help him, interpreted his dreams as being the adventures of himself outside his body. Long before this he had learned that he had a personality, was a thing apart, just as children today reach a moment when they realize that they are persons. This thing which was himself which wandered in dreams he called his soul. Soon he gave soul to all things and thus arose animism—the first of all the religions this world had seen and the seed from which all others have sprung.

But he reasoned, and he was logical. If the soul left the body in sleep, did it not also leave it at death? Hence the belief in immortality. There was only a step further to the dead talking to the living. This was the origin and source of spiritualism. But in present day savages, in early history, and probably in primitive man, this talking by the dead to the living was not a thing longed for but dreaded. The dead gave messages, not from loving sons, but of another kind.

It was interesting that spiritualism and occultism in general seemed to have been widespread in the first century after Christ, and certainly waxed fat and grew in revolutionary France, in England after the Crimean War, after our Civil War and after the World War. Why? Because such times are times of intellectual anarchy, emotionalism and moral breakdown. Today the world is sick and many men when sick become like children. Such men cast off rationalism and revert to slavery of the emotions. Man was a feeling, not a thinking, animal at best, and today a large number of people have thrown off the most recently acquired characteristic, reason, and are obeying the emotional will to believe. When, if ever, the pendulum ceases to swing, we shall all agree that there are many things concerning which it is wise to be agnostic, and some things that we cannot know. When intellect rules we shall study only phenomena, we shall not try to know realities, for reason is modest and knows its limitations.

FOLIE A DEUX. Dr. John H. W. Rhein.

Dr. Rhein reported three instances of folie à deux, a well recognized but comparatively rare form of insanity. In the first instance, a man, in apparently good health and of normal mentality, a short time after his wife developed paranoid delusions, ideas of reference and visual and auditory hallucinations, developed the same type of psychosis. In these patients there was present a paranoid state with ideas of reference and hallucinations of hearing and sight in persons who previously had not been psychotic, occurring in the presenile period in both instances. The patients had the same delusions, occur-

ring first in the wife, whose personality was the dominating one, neither exhibiting deterioration, disorientation or marked changes in personality, judgment or affectivity or pronounced changes in the arterial system; no physical basis could be found to explain a possible toxic origin of the symptoms. The cases illustrated the type of case described by the French as folie imposée.

The second illustration of this disease was the case of two sisters living intimately under the same condition, that of cook and maid, for twenty years, who had developed similar psychoses of paranoid type, the primary psychosis occurring in the stronger personality and imposing on the sister a similar secondary psychosis of the folie imposée type.

The third illustration of this disease was its occurrence in a woman 43 years of age, who developed a psychosis characterized by paranoid ideas, ideas of reference and auditory hallucinations. She had slept in the same room as her mother and sister for sixteen years. Six weeks after the first symptoms of her psychosis, the mother became insane, showing paranoid ideas, visual hallucinations and grandiose ideas which terminated shortly in cerebral hemorrhage. A second daughter contracted a similar train of symptoms as those presented by her sister. A third daughter, after a period of confusion of two months' duration, fell out the window while walking in her sleep. In this group of cases, the insanity of the mother was regarded as an instance of folie simultanée, while the secondary psychosis in the sister illustrated the type of psychosis described as folie imposée.

Folie à deux, to which the first reference in literature by Hoffman dates back to 1846, was described by the French as consisting of three types, namely, folie imposée, folie simultanée and folie communiquée.

1. La folie imposée is one in which one individual affected with a psychosis transmits to another with whom he is living intimately and in secluded association a similar psychosis in which, when the two subjects are separated, the latter recovers.

2. By folie simultanée is meant that psychosis in which two subjects are simultaneously affected by the same psychosis arising from the same external factors, in which, therefore, transmission plays no part.

3. Folie communiquée represents a psychosis in which the mental symptoms of the primary subject become firmly rooted in the second subject, but in both cases new elements arise, and a true independent psychosis occurs, which persists and progresses even after separation from the active factor.

References to the literature were cited, illustrating the various types of this psychosis, also the rôle played by heredity and contagion. Illustrations of this disease are found occurring in mother and daughter, husband and wife, brothers and sisters and also in persons closely associated but not related. Instances of folie gemillaire which may take the form of folie à deux also are cited, though in most instances this type is an example of a psychosis of different origin.

Dr. Rhein concludes that it is apparent that there are several types of insanities which occur simultaneously in two persons who have been closely associated. In twins induced insanity may be observed, as well as a coincidental occurrence of insanity, instances of which are familiar as occurring in families in which predisposition and similar exciting environmental influences play important etiologic parts. Dr. Rhein also gave instances of insanity occurring simultaneously in two persons intimately associated, which may be viewed as examples of insanity of independent etiology. Insanities also occur in two persons living together in close association in which the secondary

psychosis resembles exactly the primary one, which appears to be the direct result of contagion or suggestion without any apparent hereditary basis, and which assumes in most instances a paranoid state in which the prognosis for the secondary psychosis is good.

CHRONIC PSYCHOPATHIC INFERIORS—A DIAGNOSTIC PROBLEM.

Dr. Alice E. Johnson.

Dr. Johnson said that this group was not well-defined and in reality was undiagnosed. An effort was made to analyze a large number of patients placed in this group, with reference to the cause of their inadjustability; the difficulty of all such cases lay in the personality of the patients. The test of normality was the degree of adjustability to ordinary circumstances. Adjustability was determined by the patient's fear reaction or ability to remember pain. Moral impression ability was a good working name for the quality. The group studied showed that people have either too much or too little fear reaction; hence there are two opposite reasons for failure to make an adjustment. This is true regardless of the intellectual ability of the patient. Diagnosis should be made on this basis, and it would be found that the patients in this group suffered from two very different conditions. To those with deficient moral impressionability the name constitutional psychopathic inferior should be applied exclusively. The others are psychoneurotics. Exact diagnosis is the only basis for effective treatment. True constitutional psychopathic inferiors are incurable, and a problem for the state. There is some hope for the psychoneurotics if clinical technic is properly developed. Dr. Johnson said she thought that there is great need for a closer and more extensive study of this large class of social misfits.

Book Reviews

DER ANETHISCHE SYMPTOMENKOMPLEX. EINE STUDIE ZUR PSYCHOPATHOLOGIE DER HANDLUNG. Von Dr. Othmar Albrecht. Abhandlungen aus der Neurologie, Psychiatrie, Psychologie und ihren Grenzgebeiten. No. 12, pp. 107. Berlin: S. Karger.

In a semiphilosophical and semipsychologic general discussion of thirty-five pages, Albrecht arrives at the formulation of anethical action as the expression of a "disorder of orientation in the ethical space." He then takes up the symptoms as dependent on special mood disorders, such as exaggerations of the instinctive life and of the ego feeling, and the negativistic reactions. He summarizes the symptoms in forty cases which are given in full on pages 65 to 100, and offers the following conclusion:

"The disorientation in the social space which shows in the form of pathologically anethical activity can in a large number of cases be traced to morbid disorders of the course of reactions of the total personality. The most essential ones of these disorders can be formulated as the anethical symptom complex: The alteration of mood and emotion, the exaggeration of the instinctive life, of the self-feeling and the negativistic reaction."

The concept does not serve as a real diagnosis, any more than does "moral insanity." (See the article in Baldwin's "Dictionary of Philosophy and Psychology.") Albrecht's contribution does not clear the horizon. In the main, the characterization of the concrete plain facts entering into the individual cases and the discussions by Healy, Campbell and others, on a frankly pragmatic basis, give more satisfaction than the efforts to get light from general discussions. The records are certainly not overloaded by intelligence tests; on the other hand, one also misses the pragmatic trying out of the cases in the light of efforts at their disposal.

UEBER DIE ENTSTEHUNG DER NEGRISCHEN KORPERCHEN. Von Dr. Ladislaus Benedek und Dr. Franz Oskar Porsche. Abhandlungen aus der Neurologie, Psychiatrie, Psychologie und ihren Grenzgebeiten; Beiheft zur Monatschrift für Psychiatrie und Neurologie, herausgegeben von K. Bonhoeffer. No. 14. Pp. 86. Berlin: S. Karger, 1921.

In a study of the Negri bodies of street rabies and experimental rabies the authors have developed three methods which give a remarkably distinctive differentiation of the acidophilous parts of the structure. The descriptions and the analysis of the literature led them to make the assertion that the typical forms of the Negri bodies can be derived from the structural changes of the nucleoli. They found increased immigration of nucleoli into the cell bodies. The small homogeneous inclusions found in the Negri bodies are probably derived from the acidophilous and basophilous lumps (Schollen) suspended in the nuclear substance. The immigration of the nucleolus is promptly followed by the formation of a new nucleolus. The process of this replacement appears to be accelerated in rabies. Ten plates, most of them colored, furnish the documentary evidence. An interesting bibliography of great value to those studying cell alterations and the formation of "parasites" is appended.

OSSERVAZIONI NEUROLOGICHE SU LESIONI DEL SISTEMA NERVOSO DA TRAUMI DI GUERRA. Prof. Ottorino Rossi. Pp. 1-224. Sassari, 1921.

Prof. Ottorino Rossi in an evidently privately printed review of his war material gives, in 224 pages, a most valuable and interesting survey of casuistics—with 164 figures in the text—partly lesions of the forebrain (frontal, parietal, temporal, occipital, callosal), partly of the cerebellum, and various cerebral syndromes. The second part of the work is principally devoted to lesions of the spinal cord and spinal roots, reflex disorders, sensibility paths, etc. The individual studies are well presented. Unfortunately, there is no index, and there are no summaries which would render in a concise form the deductions from this casuistic treasure house. Those working up war material should not omit a careful study of this well reported material.